

Based upon the consensus sequences obtained as described above, oligonucleotides were then synthesized and used to identify by PCR a cDNA library that contained the sequence of interest and for use as probes to isolate a clone of the full-length coding sequence for a PRO polypeptide. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

#### EXAMPLE 2: Isolation of cDNA clones by Amylase Screening

##### 1. Preparation of oligo dT primed cDNA library

mRNA was isolated from a human tissue of interest using reagents and protocols from Invitrogen, San Diego, CA (Fast Track 2). This RNA was used to generate an oligo dT primed cDNA library in the vector pRK5D using reagents and protocols from Life Technologies, Gaithersburg, MD (Super Script Plasmid System). In this procedure, the double stranded cDNA was sized to greater than 1000 bp and the SalI/NotI linked cDNA was cloned into XhoI/NotI cleaved vector. pRK5D is a cloning vector that has an sp6 transcription initiation site followed by an SfiI restriction enzyme site preceding the XhoI/NotI cDNA cloning sites.

##### 2. Preparation of random primed cDNA library

A secondary cDNA library was generated in order to preferentially represent the 5' ends of the primary cDNA clones. Sp6 RNA was generated from the primary library (described above), and this RNA was used to generate a random primed cDNA library in the vector pSST-AMY.0 using reagents and protocols from Life Technologies (Super Script Plasmid System, referenced above). In this procedure the double stranded cDNA was sized to 500-1000 bp, linked with blunt to NotI adaptors, cleaved with SfiI, and cloned into SfiI/NotI cleaved vector. pSST-AMY.0 is a cloning vector that has a yeast alcohol dehydrogenase promoter preceding the cDNA cloning sites and the mouse amylase sequence (the mature sequence without the secretion signal) followed by the yeast alcohol dehydrogenase terminator, after the cloning sites. Thus, cDNAs cloned into this vector that are fused in frame with amylase sequence will lead to the secretion of amylase from appropriately transfected yeast colonies.

### 3. Transformation and Detection

DNA from the library described in paragraph 2 above was chilled on ice to which was added electrocompetent DH10B bacteria (Life Technologies, 20 ml). The bacteria and vector mixture was then electroporated as recommended by the manufacturer. Subsequently, SOC media (Life Technologies, 1 ml) was added and the mixture was incubated at 37°C for 30 minutes. The transformants were then plated onto 20 standard 150 mm LB plates containing ampicillin and incubated for 16 hours (37°C). Positive colonies were scraped off the plates and the DNA was isolated from the bacterial pellet using standard protocols, e.g. CsCl-gradient. The purified DNA was then carried on to the yeast protocols below.

The yeast methods were divided into three categories: (1) Transformation of yeast with the plasmid/cDNA combined vector; (2) Detection and isolation of yeast clones secreting amylase; and (3) PCR amplification of the insert directly from the yeast colony and purification of the DNA for sequencing and further analysis.

The yeast strain used was HD56-5A (ATCC-90785). This strain has the following genotype: MAT alpha, ura3-52, leu2-3, leu2-112, his3-11, his3-15, MAL<sup>+</sup>, SUC<sup>+</sup>, GAL<sup>+</sup>. Preferably, yeast mutants can be employed that have deficient post-translational pathways. Such mutants may have translocation deficient alleles in *sec71*, *sec72*, *sec62*, with truncated *sec71* being most preferred. Alternatively, antagonists (including antisense nucleotides and/or ligands) which interfere with the normal operation of these genes, other proteins implicated in this post translation pathway (e.g., SEC61p, SEC72p, SEC62p, SEC63p, TDJ1p or SSA1p-4p) or the complex formation of these proteins may also be preferably employed in combination with the amylase-expressing yeast.

Transformation was performed based on the protocol outlined by Gietz et al., Nucl. Acid. Res., 20:1425 (1992). Transformed cells were then inoculated from agar into YEPD complex media broth (100 ml) and grown overnight at 30°C. The YEPD broth was prepared as described in Kaiser et al., Methods in Yeast Genetics, Cold Spring Harbor Press, Cold Spring Harbor, NY, p. 207 (1994). The overnight culture was then diluted to about  $2 \times 10^6$  cells/ml (approx. OD<sub>600</sub>=0.1) into fresh YEPD broth (500 ml) and regrown to  $1 \times 10^7$  cells/ml (approx. OD<sub>600</sub>=0.4-0.5).

The cells were then harvested and prepared for transformation by transfer into GS3 rotor bottles in a Sorval GS3 rotor at 5,000 rpm for 5 minutes, the supernatant discarded, and then resuspended into sterile water, and centrifuged again in 50 ml falcon tubes at 3,500 rpm in a Beckman GS-6KR centrifuge. The supernatant was discarded and the cells were subsequently washed with LiAc/TE (10 ml, 10 mM Tris-HCl, 1 mM EDTA pH 7.5, 100 mM Li<sub>2</sub>OOCCH<sub>3</sub>), and resuspended into LiAc/TE (2.5 ml).

Transformation took place by mixing the prepared cells (100 µl) with freshly denatured single stranded salmon testes DNA (Lofstrand Labs, Gaithersburg, MD) and transforming DNA (1 µg, vol. < 10 µl) in microfuge tubes. The mixture was mixed briefly by vortexing, then 40% PEG/TE (600 µl, 40% polyethylene glycol-4000, 10 mM Tris-HCl, 1 mM EDTA, 100 mM Li<sub>2</sub>OOCCH<sub>3</sub>, pH 7.5) was added. This mixture was gently mixed and incubated at 30°C while agitating for 30 minutes. The cells were then heat shocked at 42°C for 15 minutes, and the reaction vessel centrifuged in a microfuge at 12,000 rpm for 5-10 seconds, decanted and resuspended into TE (500 µl, 10 mM Tris-HCl, 1 mM EDTA pH 7.5) followed by recentrifugation. The

cells were then diluted into TE (1 ml) and aliquots (200  $\mu$ l) were spread onto the selective media previously prepared in 150 mm growth plates (VWR).

Alternatively, instead of multiple small reactions, the transformation was performed using a single, large scale reaction, wherein reagent amounts were scaled up accordingly.

The selective media used was a synthetic complete dextrose agar lacking uracil (SCD-Ura) prepared as described in Kaiser et al., Methods in Yeast Genetics, Cold Spring Harbor Press, Cold Spring Harbor, NY, p. 208-210 (1994). Transformants were grown at 30°C for 2-3 days.

The detection of colonies secreting amylase was performed by including red starch in the selective growth media. Starch was coupled to the red dye (Reactive Red-120, Sigma) as per the procedure described by Biely et al., Anal. Biochem., 172:176-179 (1988). The coupled starch was incorporated into the SCD-Ura agar plates at a final concentration of 0.15% (w/v), and was buffered with potassium phosphate to a pH of 7.0 (50-100 mM final concentration).

The positive colonies were picked and streaked across fresh selective media (onto 150 mm plates) in order to obtain well isolated and identifiable single colonies. Well isolated single colonies positive for amylase secretion were detected by direct incorporation of red starch into buffered SCD-Ura agar. Positive colonies were determined by their ability to break down starch resulting in a clear halo around the positive colony visualized directly.

#### 4. Isolation of DNA by PCR Amplification

When a positive colony was isolated, a portion of it was picked by a toothpick and diluted into sterile water (30  $\mu$ l) in a 96 well plate. At this time, the positive colonies were either frozen and stored for subsequent analysis or immediately amplified. An aliquot of cells (5  $\mu$ l) was used as a template for the PCR reaction in a 25  $\mu$ l volume containing: 0.5  $\mu$ l KlenTaq (Clontech, Palo Alto, CA); 4.0  $\mu$ l 10 mM dNTP's (Perkin Elmer-Cetus); 2.5  $\mu$ l Kentaq buffer (Clontech); 0.25  $\mu$ l forward oligo 1; 0.25  $\mu$ l reverse oligo 2; 12.5  $\mu$ l distilled water. The sequence of the forward oligonucleotide 1 was:

5'-TGTAACACGACGGCCAGTTAAATAGACCTGCAATTATTAATCT-3' (SEQ ID NO:3)

The sequence of reverse oligonucleotide 2 was:

5'-CAGGAAACAGCTATGACCACCTGCACACCTGCAAATCCATT-3' (SEQ ID NO:4)

PCR was then performed as follows:

- |    |               |                  |
|----|---------------|------------------|
| a. | Denature      | 92°C, 5 minutes  |
| b. | 3 cycles of:  |                  |
|    | Denature      | 92°C, 30 seconds |
|    | Anneal        | 59°C, 30 seconds |
|    | Extend        | 72°C, 60 seconds |
| c. | 3 cycles of:  |                  |
|    | Denature      | 92°C, 30 seconds |
|    | Anneal        | 57°C, 30 seconds |
|    | Extend        | 72°C, 60 seconds |
| d. | 25 cycles of: |                  |
|    | Denature      | 92°C, 30 seconds |
|    | Anneal        | 55°C, 30 seconds |
|    | Extend        | 72°C, 60 seconds |

e.

Hold

4°C

The underlined regions of the oligonucleotides annealed to the ADH promoter region and the amylase region, respectively, and amplified a 307 bp region from vector pSST-AMY.0 when no insert was present. Typically, the first 18 nucleotides of the 5' end of these oligonucleotides contained annealing sites for the sequencing primers. Thus, the total product of the PCR reaction from an empty vector was 343 bp. However, signal sequence-fused cDNA resulted in considerably longer nucleotide sequences.

Following the PCR, an aliquot of the reaction (5 µl) was examined by agarose gel electrophoresis in a 1% agarose gel using a Tris-Borate-EDTA (TBE) buffering system as described by Sambrook et al., *supra*. Clones resulting in a single strong PCR product larger than 400 bp were further analyzed by DNA sequencing after purification with a 96 Qiaquick PCR clean-up column (Qiagen Inc., Chatsworth, CA).

#### EXAMPLE 3: Isolation of cDNA Clones Using Signal Algorithm Analysis

Various polypeptide-encoding nucleic acid sequences were identified by applying a proprietary signal sequence finding algorithm developed by Genentech, Inc. (South San Francisco, CA) upon ESTs as well as clustered and assembled EST fragments from public (e.g., GenBank) and/or private (LIFESEQ®, Incyte Pharmaceuticals, Inc., Palo Alto, CA) databases. The signal sequence algorithm computes a secretion signal score based on the character of the DNA nucleotides surrounding the first and optionally the second methionine codon(s) (ATG) at the 5'-end of the sequence or sequence fragment under consideration. The nucleotides following the first ATG must code for at least 35 unambiguous amino acids without any stop codons. If the first ATG has the required amino acids, the second is not examined. If neither meets the requirement, the candidate sequence is not scored. In order to determine whether the EST sequence contains an authentic signal sequence, the DNA and corresponding amino acid sequences surrounding the ATG codon are scored using a set of seven sensors (evaluation parameters) known to be associated with secretion signals. Use of this algorithm resulted in the identification of numerous polypeptide-encoding nucleic acid sequences.

#### EXAMPLE 4: Isolation of cDNA clones Encoding Human PRO281

In order to obtain a cDNA clone encoding PRO281, methods described in Klein et al., *Proc. Natl. Acad. Sci. USA* 93:7108-7113 (1996) were employed with the following modifications. Yeast transformation was performed with limiting amounts of transforming DNA in order to reduce the number of multiple transformed yeast cells. Instead of plasmid isolation from the yeast followed by transformation of *E. coli* as described in Klein et al., *supra*, PCR analysis was performed on single yeast colonies. PCR primers employed were bipartite in order to amplify the insert and a small portion of the invertase gene (allowing to determine that the insert was in frame with invertase) and to add on universal sequencing primer sites.

An invertase library was transformed into yeast and positives were selected on sucrose plates. Positive clones were re-tested and PCR products were sequenced. The sequence of one clone, PRO281, was determined to contain a signal peptide coding sequence. Oligonucleotide primers and probes were designed using the nucleotide sequence of PRO281. A full length plasmid library of cDNAs from human umbilical vein



endothelium tissue was titered and approximately 100,000 cfu were plated in 192 pools of 500 cfu/pool into 96-well round bottom plates. The plates were sealed and pools were grown overnight at 37°C with shaking (200rpm). PCR was performed on the individual cultures using primers. Agarose gel electrophoresis was performed and positive wells were identified by visualization of a band of the expected size. Individual positive clones were obtained by colony lift followed by hybridization with <sup>32</sup>P-labeled oligonucleotide. These clones were characterized by PCR, restriction digest, and southern blot analyses.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 80-82, and a stop signal at nucleotide positions 1115-1117 (Figure 1, SEQ ID NO:1). The predicted polypeptide precursor is 345 amino acids long, has a calculated molecular weight of approximately 37,205 daltons and an estimated pI of approximately 10.15. Analysis of the full-length PRO281 sequence shown in Figure 2 (SEQ ID NO:2) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 14, multiple transmembrane domains from about amino acid position 83 to about amino acid position 105, from about amino acid position 126 to about amino acid position 146, from about amino acid position 158 to about amino acid position 177, from about amino acid position 197 to about amino acid position 216, from about amino acid position 218 to about amino acid position 238, from about amino acid position 245 to about amino acid position 265, and from about amino acid position 271 to about amino acid position 290 and an amino acid sequence block having homology to G-protein coupled receptor proteins from about amino acid 115 to about amino acid 155. Clone UNQ244 (DNA16422-1209) has been deposited with ATCC on June 2, 1998 and is assigned ATCC deposit no. 209929.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 2 (SEQ ID NO:2), evidenced significant homology between the PRO281 amino acid sequence and the following Dayhoff sequences: H64634, AF033095\_1, B64815, YBHL\_ECOLI, EMEQUTR\_1, AF064763\_3, S53708, A69253, AF035413\_12 and S63281.

#### EXAMPLE 5: Isolation of cDNA clones Encoding Human PRO276

In order to obtain a cDNA clone encoding PRO276, methods described in Klein et al., PNAS, 93:7108-7113 (1996) were employed with the following modifications. Yeast transformation was performed with limiting amounts of transforming DNA in order to reduce the number of multiple transformed yeast cells. Instead of plasmid isolation from the yeast followed by transformation of *E. coli* as described in Klein et al., supra, PCR analysis was performed on single yeast colonies. PCR primers employed were bipartite in order to amplify the insert and a small portion of the invertase gene (allowing to determine that the insert was in frame with invertase) and to add on universal sequencing primer sites.

An invertase library was transformed into yeast and positives were selected on sucrose plates. Positive clones were re-tested and PCR products were sequenced. The sequence of one clone, PRO276, was determined to contain a signal peptide coding sequence. Oligonucleotide primers and probes were designed using the nucleotide sequence of PRO276. A full length plasmid library of cDNAs from human fetal liver cells was titered and approximately 100,000 cfu were plated in 192 pools of 500 cfu/pool into 96-well round bottom

plates. The plates were sealed and pools were grown overnight at 37 C with shaking (200rpm). PCR was performed on the individual cultures using primers. Agarose gel electrophoresis was performed and positive wells were identified by visualization of a band of the expected size. Individual positive clones were obtained by colony lift followed by hybridization with <sup>32</sup>P-labeled oligonucleotide. These clones were characterized by PCR, restriction digest, and southern blot analyses.

5 A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 180-182 and a stop signal at nucleotide positions 933-935 (Figure 3; SEQ ID NO:5). The predicted polypeptide precursor is 251 amino acids long has a calculated molecular weight of approximately 28,801 daltons and an estimated pI of approximately 9.58. The transmembrane domains are approximately at amino acids 98-116 and 152-172 of the sequence shown in Figure 4 (SEQ ID NO:6). Clone DNA16435-1208 (UNQ243) has been deposited with the ATCC and is assigned ATCC deposit no. 209930 .

10 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 4 (SEQ ID NO:6), revealed some sequence identity between the PRO276 amino acid sequence and the following Dayhoff sequences: CEG25D7\_2, ATT8O5\_2, S69696, GRHR\_RAT, NPCBAABCD\_3, AB013149\_1, P\_R85942 and AP000006\_5.

#### EXAMPLE 6: Isolation of cDNA clones Encoding Human PRO189

20 A clone designated herein as DNA14187 was isolated as described in Example 2 above from a human retina tissue library. The DNA14187 sequence is shown in Figure 7 (SEQ ID NO:9). Based on the DNA14187 sequence shown in Figure 7 (SEQ ID NO:9), oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO189. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In order to screen several libraries for a full-length clone, DNA 25 from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

A pair of PCR primers (forward and reverse) were synthesized:

30 forward PCR primer 5'-TTGACCTATACAGAGATTCATC-3' (SEQ ID NO:10); and

reverse PCR primer 5'-CTAAGAACTTCCCTCAGGATTTT-3' (SEQ ID NO:11).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA14187 sequence which had the following nucleotide sequence:

hybridization probe

5'-ATGAAGATCAATTTCAGAAGCATGCACTTCTCCTCTTGC-3' (SEQ ID NO:12).

35 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO189 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human retina tissue (LIB94). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO189 and the derived protein sequence for PRO189.

The entire nucleotide sequence of DNA21624-1391 is shown in Figure 5 (SEQ ID NO:7). Clone DNA21624-1391 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 200-202 and ending at the stop codon at nucleotide positions 1301-1303 (Figure 5). The predicted polypeptide precursor is 367 amino acids long (Figure 6). The full-length PRO189 protein shown in Figure 6 has an estimated molecular weight of about 41,871 daltons and a pI of about 5.06. Clone DNA21624-1391 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:8, the putative N-glycosylation sites are at about amino acids 224-227, 246-249 and 285-288. A domain for cytosolic fatty-acid binding proteins is at amino acids 78-107 of SEQ ID NO:8. The corresponding nucleotides can be routinely determined given the sequences provided herein.

Some sequence identity was found to W01A6.1 and F35D11.11, C. Elegans proteins, designated in a Dayhoff database as CEW01A6\_10 and CELF35D11\_11, respectively. Some sequence identity was also found to an antigen to malaria and to restin, designated in a Dayhoff database as P\_R05766 and AF014012\_1, respectively. Some sequence identity was also found to a microtubule binding protein and to myosin, designated in a Dayhoff database as AF041382\_1 and S07537, respectively. There is also some sequence identity with 1-phosphatidylinositol-4, 5-bisphosphate, designated as PIP1\_RAT.

#### EXAMPLE 7: Isolation of cDNA clones Encoding Human PRO190

A clone designated herein as DNA14232 was isolated as described in Example 2 above from a human fetal retina tissue library. The DNA14232 sequence is shown in Figure 10 (SEQ ID NO:15). Based on the DNA14232 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO190. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTATACCTACTGTAGCTTCT-3' (SEQ ID NO:16); and

reverse PCR primer 5'-TCAGAGAATTCCTTCCAGGA-3' (SEQ ID NO:17).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA14232 sequence which had the following nucleotide sequence:

hybridization probe

5'-ACAGTGCTGTAGTCATCCTGTAATATGCTCCTTGCAACA-3' (SEQ ID NO:18).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO190 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human retina tissue (LIB94). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave sequences which include the full-length DNA sequence for PRO190 [herein designated as DNA23334-1392] (SEQ ID NO:13) and the derived protein sequence for PRO190.

The entire nucleotide sequence of DNA23334-1392 is shown in Figure 8 (SEQ ID NO:13). Clone DNA23334-1392 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 193-195 and which ends at the stop codon at nucleotide positions 1465-1467 (Figure 8). The predicted polypeptide precursor is 424 amino acids long (Figure 9). The full-length PRO190 protein shown in Figure 9 has an estimated molecular weight of about 48,500 daltons and a pI of about 8.65. Clone DNA23334-1392 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:14, the putative transmembrane domains are at about amino acids 16-36, 50-74, 147-168, 229-250, 271-293, 298-318 and 328-368 of SEQ ID NO:14. N-glycosylation sites are at about amino acids 128-131, 204-207, 218-221 and 274-377 of SEQ ID NO:14. The corresponding nucleotides can be routinely determined given the sequences provided herein.

PRO190 has sequence identity with at least the following Dayhoff sequences designated as: CEZK896\_2, JC5023, GMS1\_SCHPO and S44668.

#### EXAMPLE 8: Isolation of cDNA clones Encoding Human PRO341

A clone designated herein as DNA12920 was isolated as described in Example 2 above from a human placenta tissue library. The DNA12920 sequence is shown in Figure 13 (SEQ ID NO:21). The DNA12920

sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence is herein designated DNA25314. Oligonucleotide primers based upon the DNA25314 sequence were then synthesized and employed to screen a human placenta cDNA library which resulted in the identification of the DNA26288-1239 clone shown in Figure 11. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 380-382, and a stop signal at nucleotide positions 1754-1756 (Figure 11, SEQ ID NO:19). The predicted polypeptide precursor is 458 amino acids long, has a calculated molecular weight of approximately 50,264 daltons and an estimated pI of approximately 8.17. Analysis of the full-length PRO341 sequence shown in Figure 12 (SEQ ID NO:20) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 17, transmembrane domains from about amino acid 171 to about amino acid 190, from about amino acid 220 to about amino acid 239, from about amino acid 259 to about amino acid 275, from about amino acid 286 to about amino acid 305, from about amino acid 316 to about amino acid 335, from about amino acid 353 to about amino acid 378 and from about amino acid 396 to about amino acid 417 and potential N-glycosylation sites from about amino acid 145 to about amino acid 147 and from about amino acid 155 to about amino acid 158. Clone DNA26288-1239 has been deposited with ATCC on April 21, 1998 and is assigned ATCC deposit no. 209792.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 12 (SEQ ID NO:20), evidenced homology between the PRO341 amino acid sequence and the following Dayhoff sequences: S75696, H69788, D69852, A69888, B64918, F64752, LPU89276\_1, G64962, S52977 and S44253.

#### EXAMPLE 9: Isolation of cDNA clones Encoding Human PRO180

A clone designated herein as DNA12922 was isolated as described in Example 2 above from a human placenta tissue library. The DNA12922 sequence is shown in Figure 16 (SEQ ID NO:24). The DNA12922 sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

An oligonucleotide probe was formed based upon the consensus sequence obtained above. This probe had the following sequence.

5'-ACCTGTTAGAAATGTGGTGGTTTCAGCAAGGCCTCAGTTT (SEQ ID NO:25).

This probe was used to screen a human placenta library prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp. A clone designated herein as DNA26843-1389 was obtained.

The entire nucleotide sequence of DNA26843-1389 is shown in Figure 14 (SEQ ID NO:22). Clone DNA26843-1389 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and ending at the stop codon at nucleotide positions 919-921 (Figure 14). The predicted polypeptide precursor is 266 amino acids long (Figure 15). The full-length PRO180 protein shown in Figure 15 has an estimated molecular weight of about 29,766 daltons and a pI of about 8.39. Clone DNA26843-1389 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Still analyzing the amino acid sequence of SEQ ID NO:23, the transmembrane domains are at about amino acids 13-33 (type II), 54-73, 94-113, 160-180 and 122-141 of SEQ ID NO:23. N-myristoylation sites are at about amino acids 57-62, 95-100, 99-104, 124-129 and 183-188 of SEQ ID NO:23. The corresponding nucleotides can be routinely determined given the sequences provided herein.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 15 (SEQ ID NO:23), evidenced some sequence identity between the PRO180 amino acid sequence and the following Dayhoff sequences: CEC33A11\_2, CEG11E6\_5, CELW03A5\_1 AND PEU83861\_2 (NADH dehydrogenase subunit 4L, mitochondrion).

#### EXAMPLE 10: Isolation of cDNA clones Encoding Human PRO194

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein DNA19464. Based on the DNA19464 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO194. PCR primers (forward and reverse) were synthesized based upon the DNA19464 sequence. Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA19464 sequence.

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO194 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal lung tissue (LIB25).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO194 [herein designated as DNA26844-1394] (SEQ ID NO:27) and the derived protein sequence for PRO194.

The entire nucleotide sequence of DNA26844-1394 is shown in Figure 17 (SEQ ID NO:27). Clone DNA26844-1394 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 81-83 and ending at the stop codon at nucleotide positions 873-875 (Figure 17). The predicted polypeptide precursor is 264 amino acids long (Figure 18). The full-length PRO194 protein shown in Figure 18 has an estimated molecular weight of about 29,665 daltons and a pI of about 9.34. Analysis of the full-length PRO194 sequence shown in Figure 18 (SEQ ID NO:28) evidences the presence of various important polypeptides domains as shown in Figure 18. Clone DNA26844-1394 has been deposited with ATCC on June 2, 1998 and is assigned ATCC deposit no. 209926.

Analysis of the amino acid sequence of the full-length PRO194 polypeptide suggests that it does not exhibit significant sequence similarity to any known human protein. However, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some homology between the PRO194 amino acid sequence and the following Dayhoff sequences, HUMORFT\_1, CET07F10\_5, ATFCA9\_12, F64934, YDJX\_ECOLI, ATAF00065719F29G20.19, H70002, S76980, H64934 and S76385.

#### EXAMPLE 11: Isolation of cDNA clones Encoding Human PRO203

A clone designated herein as DNA15618 was isolated as described in Example 2 above from a human fetal lung tissue library. The DNA15618 sequence is shown in Figure 21 (SEQ ID NO:31). Oligonucleotide probes were generated from the sequence of the DNA15618 molecule and were used to screen a human fetal lung library (LIB26) prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 159-161 and ending at the stop codon found at nucleotide positions 1200-1202 (Figure 19; SEQ ID NO:29). The predicted polypeptide precursor is 347 amino acids long, has a calculated molecular weight of approximately 39,870 daltons and an estimated pI of approximately 6.76. Analysis of the full-length PRO203 sequence shown in Figure 20 (SEQ ID NO:30) evidences the presence of the following: a type II transmembrane domain at about amino acid 64 to about amino acid 87; possible N-glycosylation sites at about amino acid 147 to about amino acid 150, about amino acid 155 to about amino acid 158, and about amino acid 237 to about amino acid 240; sequence identity with heavy-metal-associated domain proteins at about amino acid 23 to about amino acid 45, and sequence identity with D-isomer specific 2-hydroxyacid dehydrogenase at about amino acid 24 to about amino acid 34. Clone DNA30862-1396 was deposited with the ATCC on June 2, 1998, and is assigned ATCC deposit no. 209920.

Analysis of the amino acid sequence of the full-length PRO203 polypeptide suggests that it possesses sequence similarity to GST ATPase, thereby indicating that PRO203 may be a novel GST ATPase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO203 amino acid sequence and the following Dayhoff sequences, AF008124\_1, CFRCD1GEN\_1, and P\_R82566.

**EXAMPLE 12: Isolation of cDNA clones Encoding Human PRO290**

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified that had homology to beige and FAN. An oligonucleotide probe based upon the identified EST sequence was then synthesized and used to screen human fetal kidney cDNA libraries in an attempt to identify a full-length cDNA clone. The oligonucleotide probe had the following sequence:

5' TGACTGCACTACCCCGTGGCAAGCTGTTGAGCCAGCTCAGCTG 3' (SEQ ID NO:34).

RNA for construction of cDNA libraries was isolated from human fetal kidney tissue. The cDNA libraries used to isolate the cDNA clones encoding human PRO290 were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science* 253:1278-1280 (1991)) in the unique XhoI and NotI.

A cDNA clone was identified and sequenced in entirety. The entire nucleotide sequence of DNA35680-1212 is shown in Figure 22 (SEQ ID NO:32). Clone DNA35680-1212 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 293-295, and a stop codon at nucleotide positions 3302-3304 (Figure 22; SEQ ID NO:32). The predicted polypeptide precursor is 1003 amino acids long.

It is currently believed that the PRO290 polypeptide is related to FAN and/or beige. Clone DNA35680-1212 has been deposited with ATCC and is assigned ATCC deposit no. 209790. It is understood that the deposited clone has the actual correct sequence rather than the representations provided herein. The full-length PRO290 protein shown in Figure 23 has an estimated molecular weight of about 112,013 daltons and a pI of about 6.4.

**EXAMPLE 13: Isolation of cDNA Clones Encoding Human PRO874**

A consensus DNA sequence designated herein as DNA36459 was identified using phrap as described in Example 1 above. Based on the DNA36459 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the coding sequence for PRO874.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TCGTGCCCAGGGGCTGATGTGC-3' (SEQ ID NO:37); and

reverse PCR primer 5'-GTCTTTACCCAGCCCCGGGATGCG-3' (SEQ ID NO:38).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA36459 sequence which had the following nucleotide sequence:

hybridization probe

5'-GGCCTAATCCAACGTTCTGTCTTCAATCTGCAAATCTATGGGGTCCTGGG-3' (SEQ ID NO:39).

In order to screen several libraries for a source of a clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate



clones encoding the PRO874 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal lung tissue (LIB25).

DNA sequencing of the clones isolated as described above gave the DNA sequence for PRO874 [herein designated as DNA40621-1440] (SEQ ID NO:35) and the derived protein sequence for PRO874.

The entire nucleotide sequence of DNA40621-1440 is shown in Figure 24 (SEQ ID NO:35). Clone DNA40621-1440 contains a single open reading frame ending at the stop codon at nucleotide positions 964-966 (Figure 24). The predicted polypeptide encoded by DNA40621-1440 is 321 amino acids long (Figure 25). The PRO874 protein shown in Figure 25 has an estimated molecular weight of about 36,194 daltons and a pI of about 9.85. Analysis of the PRO874 sequence shown in Figure 25 (SEQ ID NO:36) evidenced the presence of the following: a type II transmembrane domain at about amino acids 57-80; additional transmembrane domains at about amino acids 110-126, 215-231, and 254-274; potential N-glycosylation sites at about amino acids 16-19, 27-30, and 289-292; sequence identity with hypothetical YBR002c family proteins at about amino acids 276-287; and sequence identity with ammonium transporter proteins at about amino acids 204-230. Clone DNA40621-1440 was deposited with the ATCC on June 2, 1998, and is assigned ATCC deposit no. 209922.

Analysis of the amino acid sequence of the PRO874 polypeptide suggests that it is a novel multi-span transmembrane protein. However, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO874 amino acid sequence and the following Dayhoff sequences: S67049, AF054839\_1, S73437, S52460, and HIVU80570\_1.

#### EXAMPLE 14: Isolation of cDNA Clones Encoding Human PRO710

A yeast screening assay was employed to identify cDNA clones that encoded potential secreted proteins. Use of this yeast screening assay allowed identification of a single cDNA clone whose sequence (herein designated as DNA38190) is shown in Figure 28 (SEQ ID NO:42). Based on the DNA38190 sequence shown in Figure 28, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO710. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

forward PCR primer      5'-TTCCGCAAAGAGTTCTACGAGGTGG-3' (SEQ ID NO:43)

reverse PCR primer      5'-ATTGACAACATTGACTGGCCTATGGG-3' (SEQ ID NO:44)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA38190 sequence which had the following nucleotide sequence

hybridization probe

5'-GTGGATGCTCTGTGTGCGTGCAAGATCCTTCAGGCCTTGTCCAGTGTGA-3' (SEQ ID NO:45)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO710 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 67-69 and ending at the stop codon found at nucleotide positions 1765-1767 (Figure 26, SEQ ID NO:40). The predicted polypeptide precursor is 566 amino acids long, has a calculated molecular weight of approximately 65,555 daltons and an estimated pI of approximately 5.44. Analysis of the full-length PRO710 sequence shown in Figure 27 (SEQ ID NO:41) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 32, a transmembrane domain from about amino acid 454 to about amino acid 476, an aminoacyl-transfer RNA synthetase class-II signature sequence from about amino acid 6 to about amino acid 26 and potential N-glycosylation sites from about amino acid 111 to about amino acid 114, from about amino acid 146 to about amino acid 149 and from about amino acid 292 to about amino acid 295. Clone DNA44161-1434 has been deposited with ATCC on May 27, 1998 and is assigned ATCC deposit no. 209907.

Analysis of the amino acid sequence of the full-length PRO710 polypeptide suggests that it possesses significant sequence similarity to the CDC45 protein, thereby indicating that PRO710 may be a novel CDC45 homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO710 amino acid sequence and the following Dayhoff sequences, HSAJ3728\_1, CEF34D10\_1, S64939, UMU50276\_1, TRHY\_SHEEP, CELT14E8\_1, RNA1\_YEAST, LVU89340\_1, HSU80736\_1 and CEZK337\_2.

#### EXAMPLE 15: Isolation of cDNA clones Encoding Human PRO1151

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA40665. Based on the DNA40665 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1151.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CCAGACGCTGCTCTTCGAAAGGGTC-3' (SEQ ID NO:48)

reverse PCR primer 5'-GGTCCCCGTAGGCCAGGTCCAGC-3' (SEQ ID NO:49)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40665 sequence which had the following nucleotide sequence

hybridization probe

5'-CTACTTCTTCAGCCTCAATGTGCACAGCTGGAATTACAAGGAGACGTACG-3' (SEQ ID NO:50)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1151 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1151 (designated herein as DNA44694-1500 [Figure 29, SEQ ID NO:46]; and the derived protein sequence for PRO1151.

The entire nucleotide sequence of DNA44694-1500 is shown in Figure 29 (SEQ ID NO:46). Clone DNA44694-1500 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 272-274 and ending at the stop codon at nucleotide positions 1049-1051 (Figure 29). The predicted polypeptide precursor is 259 amino acids long (Figure 30). The full-length PRO1151 protein shown in Figure 30 has an estimated molecular weight of about 28,770 daltons and a pI of about 6.12. Analysis of the full-length PRO1151 sequence shown in Figure 30 (SEQ ID NO:47) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 20, a potential N-glycosylation site from about amino acid 72 to about amino acid 75 and amino acid sequence blocks having homology to C1q domain-containing proteins from about amino acid 144 to about amino acid 178, from about amino acid 78 to about amino acid 111 and from about amino acid 84 to about amino acid 117. Clone UNQ581 (DNA44694-1500) has been deposited with ATCC on August 11, 1998 and is assigned ATCC deposit no. 203114.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 30 (SEQ ID NO:47), evidenced significant homology between the PRO1151 amino acid sequence and the following Dayhoff sequences: ACR3\_HUMAN, HP25\_TAMAS, HUMC1QB2\_1, P\_R99306, CA1F\_HUMAN, JX0369, CA24\_HUMAN, S32436, P\_R28916 and CA54\_HUMAN.

EXAMPLE 16: Isolation of cDNA clones Encoding Human PRO1282

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein as DNA33778. Based on the DNA33778 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1282.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'TCTTCAGCCGCTTGCGCAACCTC3' (SEQ ID NO:53); and

reverse PCR primer 5'TTGCTCACATCCAGCTCCTGCAGG3' (SEQ ID NO:54).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA33778 sequence which had the following nucleotide sequence:

hybridization probe

5'TGGATGTTGTCCAGACAACCAGCTGGAGCTGTATCCGAGGC3' (SEQ ID NO:55).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1282 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1282 (designated herein as DNA45495-1550 [Figure 31, SEQ ID NO:51]; and the derived protein sequence for PRO1282.

The entire coding sequence of PRO1282 is shown in Figure 31 (SEQ ID NO:51). Clone DNA45495-1550 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 120-122, and an apparent stop codon at nucleotide positions 2139-2141 (SEQ ID NO:51). The predicted polypeptide precursor is 673 amino acids long. The signal peptide is at about amino acids 1-23; the transmembrane domain is at about amino acids 579-599; an EGF-like domain cysteine pattern signature starts at about amino acid 430; and leucine zipper patterns start at about amino acids 197 and 269 of SEQ ID NO:52, see Figure 32. Clone DNA45495-1550 has been deposited with the ATCC and is assigned ATCC deposit no. 203156. The full-length PRO1282 protein shown in Figure 32 has an estimated molecular weight of about 71,655 daltons and a pI of about 7.8.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 32 (SEQ ID NO:52), revealed sequence identity between the PRO1282 amino acid sequence and the following Dayhoff sequences (data from database incorporated by reference): AB007876\_1, RNPLGPV\_1, MUSLRRP\_1, ALS\_PAPPA, AC004142\_1, ALS\_HUMAN, AB014462\_1, DMTARTAN\_1, HSCHON03\_1 and S46224.

EXAMPLE 17: Isolation of cDNA clones Encoding Human PRO358

Using the method described in Example 1 above, a single EST sequence was identified in the Incyte database, designated herein as INC3115949. Based on the INC3115949 EST sequence, oligonucleotides were synthesized to identify by PCR a cDNA library that contained the sequence of interest and for use as probes to isolate a clone of the full-length coding sequence for PRO358.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TCCCACCAGGTATCATAACTGAA-3' (SEQ ID NO:58)

reverse PCR primer 5'-TTATAGACAATCTGTTCTCATCAGAGA-3' (SEQ ID NO:59)

A probe was also synthesized:

5'-AAAAAGCATACTTGAATGGCCCAAGGATAGGTGTAAATG-3' (SEQ ID NO:60)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used

to isolate clones encoding the PRO358 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human bone marrow (LIB256). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO358 (Figure 33, SEQ ID NO:56) and the derived protein sequence for PRO358 (Figures 34, SEQ ID NO:57).

The entire nucleotide sequence of the clone identified (DNA47361-1154) is shown in Figure 33 (SEQ ID NO:56). Clone DNA47361-1154 contains a single open reading frame with an apparent translational initiation site (ATG start signal) at nucleotide positions underlined in Figure 33. The predicted polypeptide precursor is 811 amino acids long, including a putative signal sequence (amino acids 1 to 19), an extracellular domain (amino acids 20 to 575, including leucine rich repeats in the region from position 55 to position 575), a putative transmembrane domain (amino acids 576 to 595). Clone DNA47361-1249 has been deposited with ATCC and is assigned ATCC deposit no. 209431.

#### EXAMPLE 18: Isolation of cDNA clones Encoding Human PRO1310

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein as DNA37164. Based on the DNA37164 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1310.

PCR primers (forward and reverse) were synthesized:  
forward PCR primer: 5'GTTCTCAATGAGCTACCCGTCCCC3' (SEQ ID NO:63) and  
reverse PCR primer: 5'CGCGATGTAGTGGAAGCTCGGGCTC3' (SEQ ID NO:64).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47394 sequence which had the following nucleotide sequence:

hybridization probe:

5'ATCCGCATAAACCCCTCAGTCCTGGTTTGATAATGGGAGCATCTGCATGAG3' (SEQ ID NO:65).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1310 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1310 and the derived protein sequence for PRO1310.

The entire coding sequence of PRO1310 is shown in Figure 35 (SEQ ID NO:61). Clone DNA47394-1572 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 326-328, and an apparent stop codon at nucleotide positions 2594-2596 (SEQ ID NO:61). The predicted polypeptide precursor is 765 amino acids long. The signal peptide is at about amino acids 1-25 of SEQ ID NO:62. Clone DNA47394-1572 has been deposited with ATCC and is assigned ATCC deposit no. 203109.

5 The full-length PRO1310 protein shown in Figure 36 has an estimated molecular weight of about 85,898 daltons and a pI of about 6.87.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 36 (SEQ ID NO:62), revealed sequence identity between the PRO1310 amino acid sequence and the following Dayhoff sequences: AF017639\_1, P\_W36817, JC5256, CBPH\_HUMAN, MMU23184\_1, CBPN\_HUMAN, HSU83411\_1, CEF01D4\_7, RNU62897\_1 and P\_W11851.

10

#### EXAMPLE 19: Isolation of cDNA Clones Encoding Human PRO698

A yeast screening assay was employed to identify cDNA clones that encoded potential secreted proteins. Use of this yeast screening assay allowed identification of a single cDNA clone whose sequence (herein designated as DNA39906) is shown in Figure 39 (SEQ ID NO:68). Based on the DNA39906 sequence shown in Figure 39, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO698. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

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PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-AGCTGTGGTCATGGTGGTGTGGTG-3' (SEQ ID NO:69)

reverse PCR primer 5'-CTACCTTGCCATAGGTGATCCGC-3' (SEQ ID NO:70)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA39906 sequence which had the following nucleotide sequence

hybridization probe

5'-CATCAGCAAACCGTCTGTGGTTCAGCTCAACTGGAGAGGGTT-3' (SEQ ID NO:71)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO698 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human bone marrow tissue (LIB255). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or

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pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 14-16 and ending at the stop codon found at nucleotide positions 1544-1546 (Figure 37, SEQ ID NO:66). The predicted polypeptide precursor is 510 amino acids long, has a calculated molecular weight of approximately 57,280 daltons and an estimated pI of approximately 5.61. Analysis of the full-length PRO698 sequence shown in Figure 38 (SEQ ID NO:67) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 20, potential N-glycosylation sites from about amino acid 72 to about amino acid 75, from about amino acid 136 to about amino acid 139, from about amino acid 193 to about amino acid 196, from about amino acid 253 to about amino acid 256, from about amino acid 352 to about amino acid 355 and from about amino acid 411 to about amino acid 414 an amino acid block having homology to legume lectin beta-chain proteins from about amino acid 20 to about amino acid 39 and an amino acid block having homology to the HBGF/FGF family of proteins from about amino acid 338 to about amino acid 365. Clone DNA48320-1433 has been deposited with ATCC on May 27, 1998 and is assigned ATCC deposit no. 209904.

Analysis of the amino acid sequence of the full-length PRO698 polypeptide suggests that it possesses significant sequence similarity to the olfactomedin protein, thereby indicating that PRO698 may be a novel olfactomedin homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO698 amino acid sequence and the following Dayhoff sequences, OLFM\_RANCA, I73637, AB006686S3\_1, RNU78105\_1, RNU72487\_1, P\_R98225, CELC48E7\_4, CEF11C3\_3, XLU85970\_1 and S42257.

#### EXAMPLE 20: Isolation of cDNA Clones Encoding Human PRO732

A yeast screening assay was employed to identify cDNA clones that encoded potential secreted proteins. Use of this yeast screening assay allowed identification of a single cDNA clone whose sequence (herein designated as DNA42580) is shown in Figure 45 (SEQ ID NO:77). The DNA42580 sequence was then compared to a variety of known EST sequences to identify homologies. The EST databases employed included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)) as a comparison to a 6 frame translation of the EST sequence. Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

Using the above analysis, a consensus DNA sequence was assembled relative to other EST sequences using phrap. This consensus sequence is herein designated consen01. Proprietary Genentech EST sequences were employed in the consensus assembly and they are herein designated DNA20239 (Figure 42; SEQ ID NO:74), DNA38050 (Figure 43; SEQ ID NO:75) and DNA40683 (Figure 44; SEQ ID NO:76).

Based on the consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO732. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-ATGTTTGTGTGGAAGTGCCCCG-3' (SEQ ID NO:78)

forward PCR primer 5'-GTCAACATGCTCCTCTGC-3' (SEQ ID NO:79)

reverse PCR primer 5'-AATCCATTGTGCACTGCAGCTCTAGG-3' (SEQ ID NO:80)

reverse PCR primer 5'-GAGCATGCCACCACTGGACTGAC-3' (SEQ ID NO:81)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA44143 sequence which had the following nucleotide sequence

hybridization probe

5'-GCCGATGCTGTCCTAGTGGAAACAACCTCCACTGTAAGTAGATTGATCTATGCAC-3' (SEQ ID NO:82)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO732 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human fetal lung tissue (LIB26). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 88-90 and ending at the stop codon found at nucleotide positions 1447-1449 (Figure 40, SEQ ID NO:72). The predicted polypeptide precursor is 453 amino acids long, has a calculated molecular weight of approximately 50,419 daltons and an estimated pI of approximately 5.78. Analysis of the full-length PRO732 sequence shown in Figure 41 (SEQ ID NO:73) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, transmembrane domains from about amino acid 37 to about amino acid 57, from about amino acid 93 to about amino acid 109, from about amino acid 126 to about amino acid 148, from about amino acid 151 to about amino acid 172, from about amino acid 197 to about amino acid 215, from about amino acid 231 to about amino acid 245, from about



amino acid 260 to about amino acid 279, from about amino acid 315 to about amino acid 333, from about amino acid 384 to about amino acid 403 and from about amino acid 422 to about amino acid 447, potential N-glycosylation sites from about amino acid 33 to about amino acid 36, from about amino acid 34 to about amino acid 37, from about amino acid 179 to about amino acid 183, from about amino acid 298 to about amino acid 301, from about amino acid 337 to about amino acid 340 and from about amino acid 406 to about amino acid 409, an amino acid block having homology to the MIP family of proteins from about amino acid 119 to about amino acid 149 and an amino acid block having homology to DNA/RNA non-specific endonuclease proteins from about amino acid 279 to about amino acid 286. Clone DNA48334-1435 has been deposited with ATCC on June 2, 1998 and is assigned ATCC deposit no. 209924.

Analysis of the amino acid sequence of the full-length PRO732 polypeptide suggests that it possesses significant sequence similarity to the Diff33 protein, thereby indicating that PRO732 may be a novel Diff33 homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO732 amino acid sequence and the following Dayhoff sequences, HS179M20\_2, MUSTETU\_1, CER11H6\_2, RATDRP\_1, S51256, E69226, AE000869\_1, JC4120, CYB\_PARTE and P\_R50619.

#### EXAMPLE 21: Isolation of cDNA clones Encoding Human PRO1120

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein consen0352. The consen0352 sequence was then extended using repeated cycles of BLAST and phrap to extend the consensus sequence as far as possible using the sources of EST sequences discussed above. The extended consensus sequence is designated herein as DNA34365. Based on the DNA34365 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1120.

PCR primers (forward and reverse) were synthesized:

forward PCR primers: 5'-GAAGCCGGCTGTCTGAATC-3' (SEQ ID NO:85),  
5'-GGCCAGCTATCTCCGCAG-3' (SEQ ID NO:86), 5'-AAGGGCCTGCAAGAGAAG-3' (SEQ ID NO:87), 5'-CACTGGGACAACGTGTGGG-3' (SEQ ID NO:88),  
5'-CAGAGGCAACGTGGAGAG-3' (SEQ ID NO:89), and  
5'-AAGTATTGTCATACAGTGTTTC-3' (SEQ ID NO:90);  
reverse PCR primers: 5'-TAGTACTTGGGCACGAGGTTGGAG-3' (SEQ ID NO:91), and 5'-TCATACCAACTGCTGGTCATTGGC-3' (SEQ ID NO:92).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA34365 consensus sequence which had the following nucleotide sequence:

hybridization probe:

5'-CTCAAGCTGCTGGACACGGAGCGGCCGGTGAATCGGTTTCACTTG-3' (SEQ ID NO:93).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used

to isolate clones encoding the PRO1120 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1120 (designated herein as DNA48606-1479 [Figure 46, SEQ ID NO:83]; and the derived protein sequence for PRO1120.

The entire coding sequence of PRO1120 is shown in Figure 46 (SEQ ID NO:83). Clone DNA48606-1479 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 608-610 and an apparent stop codon at nucleotide positions 3209-3211. The predicted polypeptide precursor is 867 amino acids long. The full-length PRO1120 protein shown in Figure 47 has an estimated molecular weight of about 100,156 Daltons and a pI of about 9.44. Additional features of the PRO1120 polypeptide include a signal peptide at about amino acids 1-17; a sulfatase signature at about amino acids 86-98; regions of homology to sulfatases at about amino acids 87-106, 133-146, 216-229, 291-320, and 365-375; and potential N-glycosylation sites at about amino acids 65-68, 112-115, 132-135, 149-152, 171-174, 198-201, 241-245, 561-564, 608-611, 717-720, 754-757, and 764-767.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 47 (SEQ ID NO:84), revealed significant homology between the PRO1120 amino acid sequence and the following Dayhoff sequences: CELK09C4\_1, GL6S\_HUMAN, G65169, NCU89492\_1, BCU44852\_1, E64903, P\_R51355, STS\_HUMAN, GA6S\_HUMAN, and IDS\_MOUSE. Clone DNA48606-1479 was deposited with the ATCC on July 1, 1998, and is assigned ATCC deposit no. 203040.

#### EXAMPLE 22: Isolation of cDNA clones Encoding Human PRO537

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated as Incyte EST cluster no. 29605. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA48350.

In light of an observed sequence homology between the DNA48350 consensus sequence and an EST sequence encompassed within the Merck EST clone no. R63443, the Merck EST clone R63443 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 48 and is herein designated as DNA49141-1431.

Clone DNA49141-1431 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 97-99 and ending at the stop codon at nucleotide positions 442-444 (Figure 48).

The predicted polypeptide precursor is 115 amino acids long (Figure 49). The full-length PRO537 protein shown in Figure 49 has an estimated molecular weight of about 13,183 daltons and a pI of about 12.13. Analysis of the full-length PRO537 sequence shown in Figure 49 (SEQ ID NO:95) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 31, a potential N-glycosylation site from about amino acid 44 to about amino acid 47, potential N-myristoylation sites from about amino acid 3 to about amino acid 8 and from about amino acid 16 to about amino acid 21 and an amino acid block having homology to multicopper oxidase proteins from about amino acid 97 to about amino acid 105. Clone DNA49141-1431 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203003.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 49 (SEQ ID NO:95), evidenced homology between the PRO537 amino acid sequence and the following Dayhoff sequences: A54523, CELF22H10\_2, FKH4\_MOUSE, OTX1\_HUMAN, URB1\_USTMA, KNOB\_PLAFN, A32895\_1, AF036332\_1, HRG\_HUMAN and HRP3\_PLAFS.

#### EXAMPLE 23: Isolation of cDNA clones Encoding Human PRO536

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated herein as ss.clu2437.init. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA48351.

In light of an observed sequence homology between the DNA48351 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H11129, the Merck EST clone H11129 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 50 and is herein designated as DNA49142-1430.

Clone DNA49142-1430 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 48-50 and ending at the stop codon at nucleotide positions 987-989 (Figure 50). The predicted polypeptide precursor is 313 amino acids long (Figure 51). The full-length PRO536 protein shown in Figure 51 has an estimated molecular weight of about 34,189 daltons and a pI of about 4.8. Analysis of the full-length PRO536 sequence shown in Figure 51 (SEQ ID NO:97) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25, a potential N-glycosylation site from about amino acid 45 to about amino acid 48 and an amino acid sequence block having homology to sulfatase proteins from about amino acid 16 to about amino acid 26. Clone DNA49142-1430 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203002.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 51 (SEQ ID NO:97), evidenced homology between the PRO536 amino acid sequence and the following Dayhoff sequences: APU46857\_1, PK2\_DICDI, H64743, F5I14\_18, CEAM\_ECOLI, GEN14267, H64965, TCU39815\_1, PSBJ\_ODOSI and P\_R06980.

5 EXAMPLE 24: Isolation of cDNA clones Encoding Human PRO535

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated herein as ss.clu12694.init. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA48352. Two proprietary Genentech EST sequences were employed in the assembly are herein shown in Figures 54 and 55.

In light of an observed sequence homology between the DNA48352 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H86994, the Merck EST clone H86994 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 52 and is herein designated as DNA49143-1429.

Clone DNA49143-1429 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 78-80 and ending at the stop codon at nucleotide positions 681-683 (Figure 52). The predicted polypeptide precursor is 201 amino acids long (Figure 53). The full-length PRO535 protein shown in Figure 53 has an estimated molecular weight of about 22,180 daltons and a pI of about 9.68. Analysis of the full-length PRO535 sequence shown in Figure 53 (SEQ ID NO:99) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25, a transmembrane domain from about amino acid 155 to about amino acid 174, a potential N-glycosylation site from about amino acid 196 to about amino acid 199 and FKBP-type peptidyl-prolyl cis-trans isomer signature sequences from about amino acid 62 to about amino acid 77, from about amino acid 87 to about amino acid 123 and from about amino acid 128 to about amino acid 141. Clone DNA49143-1429 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203013.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST- sequence alignment analysis of the full-length sequence shown in Figure 53 (SEQ ID NO:99), evidenced homology between the PRO535 amino acid sequence and the following Dayhoff sequences: S71237, P\_R93551, P\_R28980, S71238, FKB2\_HUMAN, CELC05C8\_1, S55383, S72485, CELC50F2\_6 and S75144.

**EXAMPLE 25: Isolation of cDNA clones Encoding Human PRO718**

A cDNA sequence isolated in the amylase screen described in Example 2 (human fetal lung library) above is herein designated DNA43512 (see Figure 62; SEQ ID NO:108). The DNA43512 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA45625. Proprietary Genentech EST sequences were employed in the assembly and are herein shown in Figures 58-61.

Based on the DNA45625 sequence, oligonucleotide probes were generated and used to screen a human fetal lung library (LIB25) prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GGGTGGATGGTACTGCTGCATCC-3' (SEQ ID NO:109)

reverse PCR primer 5'-TGTTGTGCTGTGGGAAATCAGATGTG-3' (SEQ ID NO:110)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA45625 sequence which had the following nucleotide sequence:

hybridization probe

5'-GTGTCTGGAGGCTGTGGCCGTTTGTGTTTCTTGGGCTAAAATCGGG-3' (SEQ ID NO:111)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO718 gene using the probe oligonucleotide and one of the PCR primers.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 36-38 and ending at the stop codon found at nucleotide positions 607-609 (Figure 56; SEQ ID NO:102). The predicted polypeptide precursor is 157 amino acids long, has a calculated molecular weight of approximately 17,400 daltons and an estimated pI of approximately 5.78. Analysis of the full-length PRO718 sequence shown in Figure 57 (SEQ ID NO:103) evidences the presence of the following: a type II transmembrane domain from about amino acid 21 to about amino acid 40, and other transmembrane domains at about amino acid 58 to about amino acid 78, about amino acid 95 to about amino acid 114, and about amino acid 127 to about amino acid 147; a cell attachment sequence from about amino acid 79 to about amino acid 81; and a potential N-glycosylation site from about amino acid 53 to about amino acid 56. Clone DNA49647-1398 has been deposited with ATCC on June 2, 1998 and is assigned ATCC deposit no. 209919.

Analysis of the amino acid sequence of the full-length PRO718 polypeptide suggests that it possesses no significant sequence similarity to any known protein. However, an analysis of the Dayhoff database

(version 35.45 SwissProt 35) evidenced some degree of homology between the PRO718 amino acid sequence and the following Dayhoff sequences: AF045606\_1, AF039906\_1, SPBC8D2\_2, S63441, F64728, COX1\_TRYBB, F64375, E64173, RPYGJT\_3, MTCY261\_23.

**EXAMPLE 26: Isolation of cDNA clones Encoding Human PRO872**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence designated herein as clu120709.init. The clu120709.init sequence was then compared a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA48254.

In light of an observed sequence homology between the DNA48254 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3438068, the Incyte EST clone 3438068 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 63 and is the full-length DNA sequence for PRO872. Clone DNA49819-1439 was deposited with the ATCC on June 2, 1998, and is assigned ATCC deposit no. 209931.

The entire nucleotide sequence of DNA49819-1439 is shown in Figure 63 (SEQ ID NO:112). Clone DNA49819-1439 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 14-16 and ending at the stop codon at nucleotide positions 1844-1846 (Figure 63). The predicted polypeptide precursor is 610 amino acids long (Figure 64). The full-length PRO872 protein shown in Figure 64 has an estimated molecular weight of about 66,820 daltons and a pI of about 8.65. Analysis of the full-length PRO872 sequence shown in Figure 64 (SEQ ID NO:113) evidences the presence of the following features: a signal peptide at amino acid 1 to about 18, putative transmembrane domains at about amino acids 70-87, 200-222 and 568-588; sequence identity with bacterial-type phytoene dehydrogenase protein at about amino acids 71-105; sequence identity with a regulator of chromosome condensation (RCC1) signature 2 at about amino acids 201-211; leucine zipper patterns at about amino acids 214-235, 221-242, 228-249 and 364-385; a potential N-glycosylation site at about amino acids 271-274; and a glycosaminoglycan attachment site at about amino acids 75-78. Analysis of the amino acid sequence of the full-length PRO872 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO872 amino acid sequence and the following Dayhoff sequences: PRCRTI\_1, S75951, S74689, CELF37C4\_3, CRTI\_RHOCA, S76617, YNI2\_METTL, MTV014\_14, AOFB\_HUMAN, and MMU70429\_1.

**EXAMPLE 27: Isolation of cDNA clones Encoding Human PRO1063**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence designated herein as ss.clu119743.init. The Incyte EST cluster sequence

ss.clu119743.init sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA48288.

In light of an observed sequence homology between the DNA48288 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2783726, the Incyte EST clone 2783726 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 65 and is herein designated DNA49820-1427.

The full length clone shown in Figure 65 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 90-92 and ending at the stop codon found at nucleotide positions 993-995 (Figure 65; SEQ ID NO:114). The predicted polypeptide precursor is 301 amino acids long, has a calculated molecular weight of approximately 33,530 daltons and an estimated pI of approximately 4.80. Analysis of the full-length PRO1063 sequence shown in Figure 66 (SEQ ID NO:115) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 21, potential N-glycosylation sites from about amino acid 195 to about amino acid 198, from about amino acid 217 to about amino acid 220 and from about amino acid 272 to about amino acid 275, a glycosaminoglycan attachment site from about amino acid 267 to about amino acid 270, a microbodies C-terminal targeting signal site from about amino acid 299 to about amino acid 301, a type II fibronectin collagen-binding domain homology sequence from about amino acid 127 to about amino acid 168 and a fructose-bisphosphate aldolase class II protein homology sequence from about amino acid 101 to about amino acid 118. Clone DNA49820-1427 has been deposited with the ATCC on June 2, 1998 and is assigned ATCC deposit no. 209932.

Analysis of the amino acid sequence of the full-length PRO1063 polypeptide suggests that it possesses sequence similarity to the human type IV collagenase protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO1063 amino acid sequence and the following Dayhoff sequences, S68303, CFU68533\_1, P\_P91139, RNU65656\_1, PA2R\_RABIT, MMU56734\_1, FINC\_XENLA, A48925, P\_R92778 and FA12\_HUMAN.

#### EXAMPLE 28: Isolation of cDNA clones Encoding Human PRO619

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated herein as 88434. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a

BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1656694, the Incyte EST clone 1656694 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 67 and is herein designated as DNA49821-1562.

The full length clone shown in Figure 67 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 81-83 and ending at the stop codon found at nucleotide positions 450-452 (Figure 67; SEQ ID NO:116). The predicted polypeptide precursor (Figure 68, SEQ ID NO:117) is 123 amino acids long including a predicted signal peptide at about amino acids 1-20. PRO619 has a calculated molecular weight of approximately 13,710 daltons and an estimated pI of approximately 5.19. Clone DNA49821-1562 was deposited with the ATCC on June 16, 1998 and is assigned ATCC deposit no. 209981.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 68 (SEQ ID NO:117), revealed significant homology between the PRO619 amino acid sequence and the following Dayhoff sequences: S35302, D87009\_1, HSU93494\_1, HUMIGLAM5\_1, D86999\_2, HUMIGLYM1\_1, HUMIGLYMKE\_1, A29491\_1, A29498\_1, and VPR2\_MOUSE.

#### EXAMPLE 29: Isolation of cDNA clones Encoding Human PRO943

A consensus DNA sequence encoding PRO943 was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence was then extended using repeated cycles of BLAST and phrap to extend the consensus sequence as far as possible using the sources of EST sequences discussed above. The extended consensus sequence is herein designated DNA36360. Based on the DNA36360 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO943.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CGAGATGACGCCGAGCCCC-3' (SEQ ID NO:120)

reverse PCR primer 5'-CGGTTTCGACACGCGGCAGGTG-3' (SEQ ID NO:121)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA36360 sequence which had the following nucleotide sequence

hybridization probe

5'-TGCTGCTCCTGCTGCCGCCGCTGCTGCTGGGGCCTTCCCGCCGG-3' (SEQ ID NO:122)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO943 gene using the probe oligonucleotide and one of the PCR primers.



RNA for construction of the cDNA libraries was isolated from human fetal brain tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO943 (designated herein as DNA52192-1369 [Figure 69, SEQ ID NO:118]) and the derived protein sequence for PRO943.

The entire nucleotide sequence of DNA52192-1369 is shown in Figure 69 (SEQ ID NO:118). Clone DNA52192-1369 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 150-152 and ending at the stop codon at nucleotide positions 1662-1664 (Figure 69). The predicted polypeptide precursor is 504 amino acids long (Figure 70). The full-length PRO943 protein shown in Figure 70 has an estimated molecular weight of about 54,537 daltons and a pI of about 10.04. Analysis of the full-length PRO943 sequence shown in Figure 70 (SEQ ID NO:119) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 17, a transmembrane domain from about amino acid 376 to about amino acid 396, tyrosine kinase phosphorylation sites from about amino acid 212 to about amino acid 219 and from about amino acid 329 to about amino acid 336, potential N-glycosylation sites from about amino acid 111 to about amino acid 114, from about amino acid 231 to about amino acid 234, from about amino acid 255 to about amino acid 258 and from about amino acid 293 to about amino acid 296 and an immunoglobulin and MHC protein sequence homology block from about amino acid 219 to about amino acid 236. Clone DNA52192-1369 has been deposited with ATCC on July 1, 1998 and is assigned ATCC deposit no. 203042.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 70 (SEQ ID NO:119), evidenced significant homology between the PRO943 amino acid sequence and the following Dayhoff sequences: B49151, A39752, FGR1\_XENLA, S38579, RATHBFGFRB\_1, TVHU2F, FGR2\_MOUSE, CEK3\_CHICK, P\_R21080 and A27171\_1.

#### EXAMPLE 30: Isolation of cDNA clones Encoding Human PRO1188

A consensus DNA sequence was assembled relative to other EST sequences using the program "phrap" as described in Example 1 above. This consensus sequence is designated herein as DNA45679. Based on the DNA45679 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1188.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTGGTGCCTCAACAGGGAGCAG-3' (SEQ ID NO:125)

reverse PCR primer 5'-CCATTGTGCAGGTCAGGTCACAG-3' (SEQ ID NO:126)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA45679 sequence which had the following nucleotide sequence:

hybridization probe

5'-CTGGAGCAAGTGCTCAGCTGCCTGTGGTCAGACTGGGGTC-3' (SEQ ID NO:127)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1188 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1188 (designated herein as DNA52598-1518 [Figure 71, SEQ ID NO:123]); and the derived protein sequence for PRO1188.

The entire coding sequence of PRO1188 is shown in Figure 71 (SEQ ID NO:123). Clone DNA52598-1518 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 136-138 and an apparent stop codon at nucleotide positions 3688-3690. The predicted polypeptide precursor is 1184 amino acids long. The full-length PRO1188 protein shown in Figure 72 has an estimated molecular weight of about 132,582 Daltons and a pI of about 8.80. Additional features include: a signal peptide at about amino acids 1-31; an ATP/GTP binding site motif A (P-loop) at about amino acids 266-273; an aldehyde dehydrogenases cysteine active site at about amino acids 188-199; growth factor and cytokines receptors family signature 2 at about amino acids 153-159; and potential N-glycosylation sites at about amino acids 129-132, 132-135, 346-349, 420-423, 550-553, 631-634, 1000-1003, and 1056-1059.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 72 (SEQ ID NO:124), revealed significant homology between the PRO1188 amino acid sequence and the following Dayhoff sequences: SSU83114\_1, S56015, CET21B6\_4, CELT19D2\_1, and TSP1\_MOUSE.

Clone DNA52598-1518 has been deposited with ATCC and is assigned ATCC deposit no 203107.

#### EXAMPLE 31: Isolation of cDNA clones Encoding Human PRO1133

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This sequence was extended using repeated cycles of phrap. The extended consensus sequence is designated herein DNA38102. Based on the DNA38102 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1133.

PCR primers (two forward and one reverse) were synthesized:

forward PCR primer 1 5'-TCGATTATGGACGAACATGGCAGC-3' (SEQ ID NO:130);

forward PCR primer 2 5'-TTCTGAGATCCCTCATCCTC-3' (SEQ ID NO:131); and

reverse primer 5'-AGGTTTCAGGGACAGCAAGTTTGGG-3' (SEQ ID NO:132).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA38102 sequence which had the following nucleotide sequence:

hybridization probe

5'TTTGCTGGACCTCGGCTACGGAATTGGCTTCCTCTACGGACAGCTGGAT3' (SEQ ID NO:133).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with a PCR primer pair identified above. A positive library was then used to

isolate clones encoding the PRO1133 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1133 and the derived protein sequence for PRO1133.

The entire coding sequence of PRO1133 is shown in Figure 73 (SEQ ID NO:128). Clone DNA53913-1490 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 266-268 and an apparent stop codon at nucleotide positions 1580-1582 of SEQ ID NO:128. The predicted polypeptide precursor is 438 amino acids long. The signal peptide is at amino acids 1-18 of SEQ ID NO:129. EGF-like domain cysteine pattern signatures start at 315 and 385 of SEQ ID NO:129 as shown in Figure 74. Clone DNA53913-1490 has been deposited with ATCC and is assigned ATCC deposit no. 203162. The full-length PRO1133 protein shown in Figure 74 has an estimated molecular weight of about 49,260 daltons and a pI of about 6.15.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 74 (SEQ ID NO:129), revealed some sequence identity between the PRO1133 amino acid sequence and the following Dayhoff sequences (data from the database incorporated herein): AF002717\_1, LMG1\_HUMAN, B54665, UNC6\_CAEEL, LML1\_CAEEL, LMA5\_MOUSE, MMU88353\_1, LMA1\_HUMAN, HSLN2C64\_1 and AF005258\_1.

#### EXAMPLE 32: Isolation of cDNA clones Encoding Human PRO784

An initial DNA sequence (SEQ ID NO:136), referred to herein as DNA44661 and shown in Figure 77, was identified using a yeast screen, in a human fetal lung cDNA library that preferentially represents the 5' ends of the primary cDNA clones. DNA44661 was then compared to ESTs from public databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA), using the computer program BLAST or BLAST2 [Altschul et al., *Methods in Enzymology*, 266:460-480 (1996)]. The ESTs were then clustered and assembled into a consensus DNA sequence using the computer program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained is designated herein as "DNA45463". Based on the DNA45463 consensus sequence, oligonucleotides were synthesized for use as probes to isolate a clone of the full-length coding sequence for PRO784 from a human fetal lung cDNA library.

The full length DNA53978-1443 clone shown in Figure 75 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 37-39 and ending at the stop codon found at nucleotide positions 821-823 (Figure 75; SEQ ID NO:134). The predicted polypeptide precursor (Figure 76, SEQ ID NO:135) is 228 amino acids long. PRO784 has a calculated molecular weight of approximately 25,735 Daltons and an estimated pI of approximately 5.45. PRO784 has the following features: a signal peptide at about amino acid 1 to about 15; transmembrane domains at about amino acids 68 to about 87 and at about 183 to about 204; potential N-myristoylation sites at about amino acids 15-20, 51-56, 66-60, 163-168, and 206-211; and an RNP-1 protein RNA-binding region at about amino acids 108 to about 117.

Clone DNA53978-1443 was deposited with ATCC on June 16, 1998, and is assigned ATCC deposit no. 209983.

Based on a BLAST and FastA sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO784 shows amino acid sequence identity to the following proteins: RNU42209\_1, MMU91538\_1, CGU91742\_1, CELF55A4\_6, SC22\_YEAST, and F48188.

**EXAMPLE 33: Isolation of cDNA Clones Encoding Human PRO783**

A yeast screening assay was employed to identify cDNA clones that encoded potential secreted proteins. Use of this yeast screening assay allowed identification of a single cDNA clone, designated herein as DNA45201 (Figure 80; SEQ ID NO:139).

The DNA45201 sequence was then used to search expressed sequence tag (EST) databases for the presence of potential homologies. The EST databases included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained is herein designated as "consen01". A proprietary Genentech EST sequence was used in the consensus assembly and is herein designated as DNA14575 (Figure 81; SEQ ID NO:140).

Based on the consen01 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO783. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:  
forward PCR primer 5'-GACTGTATCTGAGCCCCAGACTGC-3' (SEQ ID NO:141),  
forward PCR primer 5'-TCAGCAATGAGGTGCTGCTC-3' (SEQ ID NO:142), and  
reverse PCR primer 5'-TGAGGAAGATGAGGGACAGGTTGG-3' (SEQ ID NO:143).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consen01 sequence which had the following nucleotide sequence:

hybridization probe

5'-TATGGAAGCACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCC-3' (SEQ ID NO:144).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with a PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO783 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB228). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially

available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to Sall hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

5 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO783 [herein designated as DNA53996-1442] (SEQ ID NO:137) and the derived protein sequence for PRO783.

10 The entire nucleotide sequence of DNA53996-1442 is shown in Figure 78 (SEQ ID NO:137). Clone DNA53996-1442 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 310-312 and ending at the stop codon at nucleotide positions 1777-1779 (Figure 78). The predicted polypeptide precursor is 489 amino acids long (Figure 79). The full-length PRO783 protein shown in Figure 79 has an estimated molecular weight of about 55,219 daltons and a pI of about 8.47. Analysis of the full-length PRO783 sequence shown in Figure 79 (SEQ ID NO:138) evidences the presence of the following features: transmembrane domains located at about amino acids 23-42, 67-89, 111-135, 154-176, 194-218, 15 296-319, 348-370, 387-410 and 427-452; leucine zipper patterns located at about amino acids 263-283 and 399-420; a potential tyrosine kinase phosphorylation site at about amino acids 180-187; potential N-glycosylation sites at about amino acids 105 -108 and 121-124; potential cAMP- and a cGMP-dependent protein kinase phosphorylation site at about amino acids 288-291; and a region having sequence identity with bacterial rhodopsins retinal binding site protein at about amino acids 190-218.

20 An analysis of the Dayhoff database (version 35.45 SwissProt 35) shows some sequence identity between the PRO783 amino acid sequence and the following Dayhoff sequences: YNC2\_CAEEL, D64048, ATAC002332\_3F4P9.3, NY2R\_SHEEP, and VSH\_MUMPA.

Clone DNA53996-1442 was deposited with the ATCC on June 2, 1998, and is assigned ATCC deposit no. 209921.

#### 25 EXAMPLE 34: Isolation of cDNA Clones Encoding Human PRO820

An expressed sequence tag (EST) DNA database (Merck/Wash. U) was searched and an EST designated EST no. AA504080, Merck clone 825136, was identified (library 312, human B-cell tonsil). Homology searches revealed that this EST showed sequence identity with low affinity immunoglobulin gamma Fc receptor II. DNA sequencing gave the full-length DNA sequence for PRO820 and the derived protein sequence for PRO820.

35 The entire nucleotide sequence of DNA56041-1416 is shown in Figure 82 (SEQ ID NO:145). Clone DNA56041-1416 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 115-117 and ending at the stop codon at nucleotide positions 487-489 (Figure 82). The predicted polypeptide precursor is 124 amino acids long (Figure 83). The full-length PRO820 protein shown in Figure 83 has an estimated molecular weight of about 14,080 daltons and a pI of about 7.48. Clone DNA56041-1416 has been deposited with ATCC. Regarding the sequence, it is understood that the deposited clone contains the

correct sequence, and the sequences provided herein are based on known sequencing techniques.

Still analyzing the amino acid sequence of SEQ ID NO:146, the putative signal peptide is at about amino acids 1-15 of SEQ ID NO:146. Protein kinase C phosphorylation sites are at about amino acids 20-22 and 43-45 of SEQ ID NO:146. An N-myristoylation site is at about amino acids 89-94 of SEQ ID NO:146. An immunoglobulin and major histocompatibility complex domain is at about amino acids 83-90 of SEQ ID NO:146. The corresponding nucleotides can be routinely determined given the sequences provided herein.

#### EXAMPLE 35: Isolation of cDNA Clones Encoding Human PRO1080

A consensus DNA sequence was assembled relative to other EST sequences using phrap and was extended using repeated cycles of BLAST and phrap so as to extend the consensus sequence as far as possible using the sources of the EST sequences as described in Example 1 above. The consensus sequence is designated herein as DNA52640. An EST proprietary to Genentech was employed in the consensus assembly and is herein designated as DNA36527 (Figure 86; SEQ ID NO:149).

In light of an observed sequence homology between the DNA36527 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 526423, the Merck EST clone 526423 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 84 and is herein designated as DNA56047-1456.

The entire nucleotide sequence of DNA56047-1456 is shown in Figure 84 (SEQ ID NO:147). Clone DNA56047-1456 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 159-161 and ending at the stop codon at nucleotide positions 1233-1235 of SEQ ID NO:147 (Figure 84). The predicted polypeptide precursor is 358 amino acids long (Figure 85). The full-length PRO1080 protein shown in Figure 85 has an estimated molecular weight of about 40,514 daltons and a pI of about 6.08. Clone DNA56047-1456 has been deposited with ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Also shown in Figure 85 are the approximate locations of the signal peptide, cell attachment site, Nt-DnaJ domain signature, region having sequence identity with Nt-DnaJ domain proteins, and N-glycosylation sites. The corresponding nucleic acids of these amino acid sequences and others provided herein can be routinely determined by the information provided herein.

#### EXAMPLE 36: Isolation of cDNA Clones Encoding Human PRO1079

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above, and is herein designated DNA52714. Based on information provided by the assembly, the clone for Merck EST no. HO6898 was obtained and sequenced, thereby giving the nucleotide sequence designated herein as DNA56050-1455. The entire nucleotide sequence of DNA56050-1455 is shown in Figure 87 (SEQ ID NO:150). Clone DNA56050-1455 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 183-185 and ending at the stop codon at nucleotide positions 861-863 (Figure 87). The predicted polypeptide precursor is 226 amino acids long (Figure 88). The full-

length PRO1079 protein shown in Figure 88 has an estimated molecular weight of about 24,611 Daltons and a pI of about 4.85. Analysis of the full-length PRO1079 sequence shown in Figure 88 (SEQ ID NO:3) evidences the presence of the following features: a signal peptide at about amino acid 1-29; potential N-myristoylation sites at about amino acids 10-15, and 51-56; homology to photosystem I psaG and psaK proteins at about amino acids 2 to 20; and homology to prolyl endopeptidase family serine proteins at about amino acids 150 to 163.

Analysis of the amino acid sequence of the full-length PRO1079 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced some sequence identity between the PRO1079 amino acid sequence and the following Dayhoff sequences: CEK10C3\_4, MMU50734\_1, D69503, AF051149\_1, and VSMP\_CVMS.

Clone UNQ536 (DNA56050-1455) was deposited with the ATCC on June 22, 1998, and is assigned ATCC deposit no. 203011.

#### EXAMPLE 37: Isolation of cDNA clones Encoding Human PRO793

A cDNA clone (DNA56110-1437) encoding a native human PRO793 polypeptide was identified by a yeast screen, in a human skin tumor cDNA library that preferentially represents the 5' ends of the primary cDNA clones. The yeast screen employed identified a single EST clone designated herein as DNA50177 (Figure 91; SEQ ID NO:154). The DNA50177 sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence is herein designated DNA50972.

In light of an observed sequence homology between the DNA50972 consensus sequence and an EST sequence encompassed within the Merck EST clone no. N33874, the Merck EST clone N33874 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 89 and is herein designated as DNA56110-1437.

The full-length DNA56110-1437 clone shown in Figure 89 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 77-79 and ending at the stop codon at nucleotide positions 491-493 (Figure 89). The predicted polypeptide precursor is 138 amino acids long (Figure 90). The full-length PRO793 protein shown in Figure 90 has an estimated molecular weight of about 15,426 daltons and a pI of about 10.67. Analysis of the full-length PRO793 sequence shown in Figure 90 (SEQ ID NO:153) evidences the presence of the following: transmembrane domains from about amino acid 12 to about amino acid 30, from about amino acid 33 to about amino acid 52, from about amino acid 69 to about amino acid 89 and from about amino acid 93 to about amino acid 109, potential N-myristoylation sites from about amino acid 11 to about amino acid 16, from about amino acid 51 to about amino acid 56 and from about amino acid 116

to about amino acid 121 and an amino acid sequence block having homology to an aminoacyl-transfer RNA synthetase class-II protein from about amino acid 49 to about amino acid 59. Clone DNA56110-1437 has been deposited with ATCC on August 11, 1998 and is assigned ATCC deposit no. 203113.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 90 (SEQ ID NO:153), evidenced certain homology between the PRO793 amino acid sequence and the following Dayhoff sequences: S47453, AF015193\_12, MTEHGNS9\_2, E64030, H69784, D64995, CD53\_MOUSE, GEN8006, AE001138\_7 and COX2\_STRPU.

#### EXAMPLE 38: Isolation of cDNA Clones Encoding Human PRO1016

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. The consensus sequence obtained is herein designated DNA53502.

In light of an observed sequence homology between the DNA53502 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 38680, the Merck EST clone 38680 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 92.

The entire nucleotide sequence of DNA56113-1378 is shown in Figure 92 (SEQ ID NO:155). Clone DNA56113-1378 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 168-170 and ending at the stop codon at nucleotide positions 1302-1304 (Figure 92). The predicted polypeptide precursor is 378 amino acids long (Figure 93). The full-length PRO1016 protein shown in Figure 93 has an estimated molecular weight of about 44,021 daltons and a pI of about 9.07. Clone DNA56113-1378 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO1016 polypeptide suggests that portions of it possess sequence identity with acyltransferase, thereby indicating that PRO1016 may be a novel acyltransferase.

Still analyzing the amino acid sequence of SEQ ID NO:156, the putative signal peptide is at about amino acids 1-18 of SEQ ID NO:156. The transmembrane domain(s) are at about amino acids 332-352 and 305-330 of SEQ ID NO:156. The fructose-bisphosphate aldolase class-II protein homology sequence is at about amino acids 73-90 of SEQ ID NO:156. The extradiol ring-cleavage dioxygenase protein is at about amino acids 252-275 of SEQ ID NO:156. The corresponding nucleotides can be routinely determined given the sequences provided herein.

The specific Dayhoff database designation names of sequences to which PRO1016 has sequence identity with include the following: S52645, P\_R59712, P\_R99249, P\_R59713, BNAGPATRF\_1, CELT05H4\_15 and CELZK40\_1.

#### EXAMPLE 39: Isolation of cDNA Encoding Human PRO1013

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described



in Example 1 above. The consensus DNA sequence was then extended using repeated cycles of BLAST and phrap to extend the consensus sequence as far as possible using the sources of EST sequences.

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3107695, the Incyte EST clone 3107695 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 94 and is herein designated as DNA56410-1414.

The entire nucleotide sequence of DNA56410-1414 is shown in Figure 94 (SEQ ID NO:157). Clone DNA56410-1414 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 17-19 and ending at the stop codon at nucleotide positions 1244-1246 (Figure 94). The predicted polypeptide precursor is 409 amino acids long (Figure 95). The full-length PRO1013 protein shown in Figure 95 has an estimated molecular weight of about 46,662 daltons and a pI of about 7.18. Clone DNA56410-1414 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Still analyzing the amino acid sequence of SEQ ID NO:158, the putative signal peptide is at about amino acids 1-19 of SEQ ID NO:158. N-glycosylation sites are at about amino acids 75-78 and 322-325 of SEQ ID NO:158. An N-myristoylation site is at about amino acids 184-189 of SEQ ID NO:158. A growth factor and cytokine receptor family domain is at about amino acids 134-149 of SEQ ID NO:158. The corresponding nucleotides can be routinely determined given the sequences provided herein.

Blast analysis showed some sequence identity with other proteins. Specifically, PRO1013 has some sequence identity with at least the Dayhoff sequences designated: D63877\_1; MHU22019\_1, AE000730\_10, and AF019079\_1.

#### EXAMPLE 40: Isolation of cDNA Clones Encoding Human PRO937

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. That consensus sequence is herein designated DNA49651. Based on the DNA49651 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO937.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTCCGTGGTAAACCCACAGCCC-3' (SEQ ID NO:161); and

reverse PCR primer 5'-TCACATCGATGGGATCCATGACCG-3' (SEQ ID NO:162).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA48651 sequence which had the following nucleotide sequence:

hybridization probe

5'-GGTCTCGTGACTGTGAAGCCATGTTACAACACTACTGCTCAAACATCATGAG-3' (SEQ ID NO:163).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO937 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO937 [herein designated as DNA56436-1448] (SEQ ID NO:159) and the derived protein sequence for PRO937.

The entire nucleotide sequence of DNA56436-1448 is shown in Figure 96 (SEQ ID NO:159). It contains a single open reading frame having an apparent translational initiation site at nucleotide positions 499-501 and ending at the stop codon found at nucleotide positions 2167-2169 (Figure 96, SEQ ID NO:159). The predicted polypeptide precursor is 556 amino acids long, has a calculated molecular weight of approximately 62,412 daltons and an estimated pI of approximately 6.62. Analysis of the full-length PRO937 sequence shown in Figure 97 (SEQ ID NO:160) evidences the presence of the following features: signal peptide at about amino acids 1-22; ATP/GTP-binding site motif A (P-loop) at about amino acids 515-523; a potential N-glycosylation site at about amino acids 514-517; and sites of glypican homology at about amino acids 54-74, 106-156, 238-279, 309-345, 423-459, and 468-505.

Clone DNA56436-1448 has been deposited with ATCC on May 27, 1998, and is assigned ATCC deposit no. 209902.

Analysis of the amino acid sequence of the full-length PRO937 polypeptide suggests that it possesses significant sequence similarity to glypican proteins, thereby indicating that PRO937 may be a novel glypican protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO937 amino acid sequence and the following Dayhoff sequences: GPCCK\_MOUSE, GPC2\_RAT, GPC5\_HUMAN, GPC3\_HUMAN, P\_R30168, CEC03H12\_2, GEN13820, HS119E23\_1, HDAC\_DROME, and AF017637\_1.

#### EXAMPLE 41: Isolation of cDNA clones Encoding Human PRO842

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence designated herein as Incyte EST cluster sequence no. 69572. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA54230.

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA477092, the Merck EST clone AA477092 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 98 and is herein designated as DNA56855-1447.

The full length clone shown in Figure 98 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 153-155 and ending at the stop codon found at nucleotide positions 510-512 (Figure 98; SEQ ID NO:164). The predicted polypeptide precursor (Figure 99, SEQ ID NO:165) is 119 amino acids long. PRO842 has a calculated molecular weight of approximately 13,819 Daltons and an estimated pI of approximately 11.16. Other features of PRO842 include a signal peptide at about amino acids 1-22, a potential protein kinase C phosphorylation site at about amino acids 39-41 and two potential N-myristoylation sites at about amino acids 27-32 and about amino acids 46-51.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 98 (SEQ ID NO:164), evidenced some homology between the PRO842 amino acid sequence and the following Dayhoff sequences: CEZK131\_11, P\_R80843, RAT5HT2X\_1, S81882\_1, A60912, MCU60315\_137MC137L, U93422\_1, p\_P91996, U93462\_1, and ZN18\_HUMAN.

Clone DNA56855-1447 was deposited with the ATCC on June 23, 1998, and is assigned ATCC deposit no. 203004.

#### EXAMPLE 42: Isolation of cDNA clones Encoding Human PRO839

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte LIFESEQ® database, designated Incyte EST Cluster No. 24479. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55709.

In light of an observed sequence homology between the DNA55709 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 754525, the Merck EST clone 754525 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 100 and is herein designated as DNA56859-1445.

The full length clone shown in Figure 100 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 2-4 and ending at the stop codon found at nucleotide positions 263-265 (Figure 100; SEQ ID NO:166). The predicted polypeptide precursor (Figure 101, SEQ ID NO:167) is 87 amino acids long. PRO839 has a calculated molecular weight of approximately 9,719 Daltons and an estimated pI of approximately 4.67. Other features of PRO839 include a signal peptide at about amino acids 1-23, potential protein kinase C phosphorylation sites at about amino acids 37-39 and about amino acids 85-87, a potential casein kinase II phosphorylation site at about amino acids 37-40, sequence identity with ribonucleotide reductase large subunit protein at about amino acids 50-60, and sequence identity with

eukaryotic RNA-binding region RNP-1 proteins at about amino acids 70-79.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 101 (SEQ ID NO:167), evidenced some homology between the PRO839 amino acid sequence and the following Dayhoff sequences: CD14\_MOUSE, XPR6\_YARLI, HS714385\_1, S49783, BB19\_RABIT, GVPH-HALME, AB003135\_1, P\_R85453, LUU27081\_2, and TP2B\_MOUSE.

Clone DNA56859-1445 was deposited with the ATCC on June 23, 1998, and is assigned ATCC deposit no.209019.

**EXAMPLE 43: Isolation of cDNA Clones Encoding Human PRO1180**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence (Incyte EST cluster sequence no. 14732). The Incyte EST cluster sequence no. 14732 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55711.

In light of an observed sequence homology between the DNA55711 consensus sequence and an EST sequence encompassed within the Merck EST clone no. T60981, the Merck EST clone T60981 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 102 and is herein designated DNA56860-1510.

The full length clone shown in Figure 102 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 78-80 and ending at the stop codon found at nucleotide positions 909-911 (Figure 102; SEQ ID NO:168). The predicted polypeptide precursor is 277 amino acids long, has a calculated molecular weight of approximately 31,416 daltons and an estimated pI of approximately 8.88. Analysis of the full-length PRO1180 sequence shown in Figure 103 (SEQ ID NO:169) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 23, a leucine zipper pattern sequence from about amino acid 10 to about amino acid 31, and potential N-myristylation sited from about amino acid 64 to about amino acid 69, from about amino acid 78 to about amino acid 83, from about amino acid 80 to about amino acid 85, from about amino acid 91 to about amino acid 96 and from about amino acid 201 to about amino acid 206. Clone DNA56860-1510 has been deposited with the ATCC on June 9, 1998 and is assigned ATCC deposit no. 209952.

Analysis of the amino acid sequence of the full-length PRO1180 polypeptide suggests that it possesses sequence similarity to the methyltransferase family of proteins. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO1180 amino acid

sequence and the following Dayhoff sequences, MTCI65\_14, D69267, YH09\_YEAST, BIOC\_SERMA, ATAC00448415T1D16.16, SHGCPIR\_18, SPBC3B9\_4, AB009504\_14, P\_W17977 and A69952.

**EXAMPLE 44: Isolation of cDNA clones Encoding Human PRO1134**

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 7511. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55725. Two proprietary Genentech EST sequences were employed in the assembly and are shown in Figure 106 (SEQ ID NO:172) and Figure 107 (SEQ ID NO:173).

In light of an observed sequence homology between the DNA55725 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H94897, the Merck EST clone H94897 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 106 and is herein designated as DNA56865-1491.

Clone DNA56865-1491 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 153-155 and ending at the stop codon at nucleotide positions 1266-1268 (Figure 104). The predicted polypeptide precursor is 371 amino acids long (Figure 105). The full-length PRO1134 protein shown in Figure 105 has an estimated molecular weight of about 41,935 daltons and a pI of about 9.58. Analysis of the full-length PRO1134 sequence shown in Figure 105 (SEQ ID NO:171) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 23, potential N-glycosylation sites from about amino acid 103 to about amino acid 106, from about amino acid 249 to about amino acid 252 and from about amino acid 257 to about amino acid 260, and an amino acid block having homology to tyrosinase CuA-binding region proteins from about amino acid 280 to about amino acid 306. Clone DNA56865-1491 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203022.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 105 (SEQ ID NO:171), evidenced significant homology between the PRO1134 amino acid sequence and the following Dayhoff sequences: F20P5\_18, AC002396\_10, S47847, C64146, GSPA\_BACSU, P\_W10564, RFAI\_ECOLI, Y258\_HAEIN, RFAJ\_SALTY and P\_R32985.

**EXAMPLE 45: Isolation of cDNA clones Encoding Human PRO830**

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incytedatabase, designated 20251. This EST cluster sequence was then compared

to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program “phrap” (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55733.

In light of an observed sequence homology between the DNA55733 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H78534, the Merck EST clone H78534 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 108 and is herein designated as DNA56866-1342.

Clone DNA56866-1342 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 154-156 and ending at the stop codon at nucleotide positions 415-417 (Figure 108). The predicted polypeptide precursor is 87 amino acids long (Figure 109). The full-length PRO830 protein shown in Figure 109 has an estimated molecular weight of about 9,272 daltons and a pI of about 9.19. Analysis of the full-length PRO830 sequence shown in Figure 109 (SEQ ID NO:175) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 33, potential N-myristoylation sites from about amino acid 2 to about amino acid 7 and from about amino acid 8 to about amino acid 13 and a thioredoxin family of proteins homology block from about amino acid 23 to about amino acid 39. Clone UNQ470 (DNA56866-1342) has been deposited with ATCC on June 22, 1998 and is assigned ATCC deposit no. 203023.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 109 (SEQ ID NO:175), evidenced significant homology between the PRO830 amino acid sequence and the following Dayhoff sequences: HSU88154\_1, HSU88153\_1, SAPKSGENE\_1, HPU31791\_5, GGCNOT2\_1, CPU91421\_1, CHKESTPC09\_1, PQ0769, U97553\_79 and B60095.

#### EXAMPLE 46: Isolation of cDNA clones Encoding Human PRO1115

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated Incyte EST cluster sequence no. 165008. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program “phrap” (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55726.

In light of an observed sequence homology between the DNA55726 consensus sequence and an EST sequence encompassed within the Merck EST clone no. R75784, the Merck EST clone R75784 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 111 and is herein designated as DNA56868-1478.

The full length clone shown in Figure 110 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 189-191 and ending at the stop codon found at nucleotide positions 1524-1526 (Figure 110; SEQ ID NO:176). The predicted polypeptide precursor (Figure 111, SEQ ID NO:177) is 445 amino acids long. PRO1115 has a calculated molecular weight of approximately 50,533 Daltons and an estimated pI of approximately 8.26. Additional features include a signal peptide at about amino acids 1-20; potential N-glycosylation sites at about amino acids 204-207, 295-298, and 313-316; and putative transmembrane domains at about amino acids 35-54, 75-97, 126-146, 185-204, 333-350, and 353-371.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 111 (SEQ ID NO:177), evidenced some amino acid sequence identity between the PRO1115 amino acid sequence and the following Dayhoff sequences: AF053947\_79, S73698, CEC47A10\_4, CCOMTND55G\_1, HS4LMP2AC\_1, LMP2\_EBV, PA24\_MOUSE, HCU33331\_7, P-W05508, and AF002273\_1.

Clone DNA56868-1478 was deposited with the ATCC on June 23, 1998 and is assigned ATCC deposit no. 203024..

#### EXAMPLE 47: Isolation of cDNA clones Encoding Human PRO1277

A consensus DNA sequence was assembled relative to other ESTs using repeated cycles of BLAST and the program "phrap" as described in Example 1 above. One or more of the ESTs from the assembly was derived from diseased coronary artery tissue. The consensus sequence obtained is designated herein as "DNA49434".

In light of an observed sequence homology between the DNA49434 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3042605, the Incyte EST clone 3042605 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 112 (SEQ ID NO:178).

Clone DNA56869-1545 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 188-190, and an apparent stop codon at nucleotide positions 2222-2224 (Figure 112). The predicted polypeptide precursor is 678 amino acids long (Figure 113). The full-length PRO1277 protein shown in Figure 113 has an estimated molecular weight of about 73,930 daltons and a pI of about 9.48. Additional features include a signal peptide at about amino acids 1-26; a transmembrane domain at about amino acids 181-200, and potential N-glycosylation sites at about amino acids 390-393 and 520-523.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 113 (SEQ ID NO:179), revealed significant homology between the PRO1277 amino acid sequence and Dayhoff sequence no AF012252\_1. Homology was also found between the PRO1277 amino acid sequence and the following Dayhoff sequences: AF006740\_1,

CA36\_HUMAN, HSU1\_1, HUMCOL7A1X\_1, CA17\_HUMAN, MMZ78163\_1, CAMA\_CHICK, HSU69263\_1, YNX3\_CAEEL, and MMRNAM3\_1.

Clone DNA56869-1545 has been deposited with ATCC and is assigned ATCC deposit no. 203161.

**EXAMPLE 48: Isolation of cDNA Clones Encoding Human PRO1135**

5 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA52767. Based on the DNA52767 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1135.

10 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with PCR primer pairs prepared based upon the DNA52767 sequence. A positive library was then used to isolate clones encoding the PRO1135 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human coronary artery smooth muscle tissue (LIB309). The cDNA libraries used to isolate the cDNA clones were constructed  
15 by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

20 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1135 [herein designated as DNA56870-1492] (SEQ ID NO:180) and the derived protein sequence for PRO1135.

The entire nucleotide sequence of DNA56870-1492 is shown in Figure 114 (SEQ ID NO:180). Clone DNA56870-1492 contains a single open reading frame with an apparent translational initiation site at nucleotide  
25 positions 62-64 and ending at the stop codon at nucleotide positions 1685-1687 (Figure 114). The predicted polypeptide precursor is 541 amino acids long (Figure 115). The full-length PRO1135 protein shown in Figure 115 has an estimated molecular weight of about 60,335 daltons and a pI of about 5.26. Analysis of the full-length PRO1135 sequence shown in Figure 115 (SEQ ID NO:181) evidences the presence of the following:  
30 a signal peptide from about amino acid 1 to about amino acid 21, potential N-glycosylation sites from about amino acid 53 to about amino acid 56, from about amino acid 75 to about amino acid 78, from about amino acid 252 to about amino acid 255 and from about amino acid 413 to about amino acid 416 and an amino acid block having homology to glycosyl hydrolase family 35 proteins from about amino acid 399 to about amino acid 414. Clone DNA56870-1492 has been deposited with ATCC on June 2, 1998 and is assigned ATCC deposit no. 209925.

35 Analysis of the amino acid sequence of the full-length PRO1135 polypeptide suggests that it possesses significant sequence similarity to the alpha 1,2-mannosidase protein, thereby indicating that PRO1135 may be a novel mannosidase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35)



evidenced significant homology between the PRO1135 amino acid sequence and the following Dayhoff sequences, DMC86E4\_5, D86967\_1, SPAC23A1\_4, YH04\_YEAST, B54408, SSMAN9MAN\_1, CEZC410\_4, S61631 and MSU14190\_1.

**EXAMPLE 49: Isolation of cDNA Clones Encoding Human PRO1114**

A cDNA sequence isolated in the amylase screen described in Example 2 above was found, by the WU-BLAST-2 sequence alignment computer program, to have certain sequence identity to other known interferon receptors. This cDNA sequence is herein designated DNA48466 and is shown in Figure 118 (SEQ ID NO:184). Based on the sequence identity, probes were generated from the sequence of the DNA48466 molecule and used to screen a human breast carcinoma library (LIB135) prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

The oligonucleotide probes employed were as follows:

forward PCR primer 5'-AGGCTTCGCTGCGACTAGACCTC-3' (SEQ ID NO:185)

reverse PCR primer 5'-CCAGGTCGGGTAAGGATGGTTGAG-3' (SEQ ID NO:186)

hybridization probe

5'-TTTCTACGCATTGATTCCATGTTTGCTCACAGATGAAGTGGCCATTCTGC-3' (SEQ ID NO:187)

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 250-252, and a stop signal at nucleotide positions 1183-1185 (Figure 116, SEQ ID NO:182). The predicted polypeptide precursor is 311 amino acids long, has a calculated molecular weight of approximately 35,076 daltons and an estimated pI of approximately 5.04. Analysis of the full-length PRO1114 interferon receptor sequence shown in Figure 117 (SEQ ID NO:183) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 29, a transmembrane domain from about amino acid 230 to about amino acid 255, potential N-glycosylation sites from about amino acid 40 to about amino acid 43 and from about amino acid 134 to about amino acid 137, an amino acid sequence block having homology to tissue factor proteins from about amino acid 92 to about amino acid 119 and an amino acid sequence block having homology to integrin alpha chain proteins from about amino acid 232 to about amino acid 262. Clone DNA57033-1403 has been deposited with ATCC on May 27, 1998 and is assigned ATCC deposit no. 209905.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 117 (SEQ ID NO:183), evidenced significant homology between the PRO1114 interferon receptor amino acid sequence and the following Dayhoff sequences: G01418, INR1\_MOUSE, P\_R71035, INGS\_HUMAN, A26595\_1, A26593\_1, I56215 and TF\_HUMAN.

**EXAMPLE 50: Isolation of cDNA Clones Encoding Human PRO828**

A consensus DNA sequence was identified using the method described in Example 1 above. This

consensus sequence is herein designated DNA35717. Based on the DNA35717 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO828.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GCAGGACTTCTACGACTTCAAGGC-3' (SEQ ID NO:190); and

reverse PCR primer 5'-AGTCTGGGCCAGGTACTTGAAGGC-3' (SEQ ID NO:191).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35717 sequence which had the following nucleotide sequence:

hybridization probe

5'-CAACATCCGGGGCAAACCTGGTGTCTGCTGGAGAAGTACCGCGGATCGGTGT-3' (SEQ ID NO:192)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO828 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal lung tissue (LIB25).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO828 [herein designated as DNA57037-1444] (SEQ ID NO:188) and the derived protein sequence for PRO828.

The entire nucleotide sequence of DNA57037-1444 is shown in Figure 119 (SEQ ID NO:188). Clone DNA57037-1444 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 34-36 and ending at the stop codon at nucleotide positions 595-597 (Figure 119). The predicted polypeptide precursor is 187 amino acids long (Figure 120). The full-length PRO828 protein shown in Figure 120 has an estimated molecular weight of about 20,996 daltons and a pI of about 8.62. Analysis of the full-length PRO828 sequence shown in Figure 120 (SEQ ID NO:189) evidences the presence of the following: a signal peptide at about amino acids 1- 21; sequences identity to glutathione peroxidases signature 2 at about amino acids 82-89; sequence identity to glutathione peroxidases selenocysteine proteins at about amino acids 35-60, 63-100, 107-134, and 138-159. Clone DNA57037-1444 has been deposited with ATCC on May 27, 1998, and is assigned ATCC deposit no. 209903.

Analysis of the amino acid sequence of the full-length PRO828 polypeptide suggests that it possesses significant sequence similarity to glutathione peroxidases, thereby indicating that PRO828 may be a novel peroxidase enzyme. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO828 amino acid sequence and the following Dayhoff sequences: AF053311\_1, CELT09A12\_2, AC004151\_3, BTUE\_ECOLI, CER05H10\_3, P\_P80918, PWU88907\_1, and P\_W22308.

#### EXAMPLE 51: Isolation of cDNA clones Encoding Human PRO1009

A cDNA clone (DNA57129-1413) encoding a native human PRO1009 polypeptide was identified by the use of a yeast screen, in a human SK-Lu-1 adenocarcinoma cell line cDNA library that preferentially represents the 5' ends of the primary cDNA clones. First SEQ ID NO:195 (Figure 123) was identified, which

was extended by alignments to other EST sequences to form a consensus sequence. Oligonucleotide probes based upon the consensus sequence were synthesized and used to screen the cDNA library which gave rise to the full-length DNA57129-1413 clone.

The full length DNA57129-1413 clone shown in Figure 121 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 41-43 and ending at the stop codon found at nucleotide positions 1886-1888 (Figure 121; SEQ ID NO:193). The predicted polypeptide precursor (Figure 122, SEQ ID NO:194) is 615 amino acids long. Figure 122 also shows the approximate locations of the signal sequence, transmembrane domains, myristoylation sites, a glycosylation site and an AMP-binding domain. PRO1009 has a calculated molecular weight of approximately 68,125 daltons and an estimated pI of approximately 7.82. Clone DNA57129-1413 has been deposited with ATCC and is assigned ATCC deposit no. 209977. It is understood that the deposited clone has the actual and correct sequence and that the representations herein may have minor, normal sequencing errors.

Based on a WU-BLAST-2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1009 shows amino acid sequence identity to at least the following proteins which were designated in a Dayhoff database as follows: F69893, CEF28F8\_2, BSY13917\_7, BSY13917\_7, D69187, D69649, XCRPFB\_1, E64928, YDID\_ECOLI, BNACSF8\_1 and RPU75363\_2.

#### EXAMPLE 52: Isolation of cDNA Clones Encoding Human PRO1007

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated as DNA40671.

In light of an observed sequence homology between the DNA40671 consensus sequence and an EST sequence encompassed within the Merck EST clone no. T70513, the Merck EST clone T70513 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 124.

The entire nucleotide sequence of DNA57690-1374 is shown in Figure 124 (SEQ ID NO:196). Clone DNA57690-1374 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 16-18 and ending at the stop codon at nucleotide positions 1054-1056 (Figure 124). The predicted polypeptide precursor is 346 amino acids long (Figure 125). The full-length PRO1007 protein shown in Figure 125 has an estimated molecular weight of about 35,971 daltons and a pI of about 8.17. Clone DNA57690-1374 has been deposited with the ATCC on June 9, 1998. Regarding the sequence, it is understood that the deposited clone contains the actual sequence, and the sequences provided herein are based on known sequencing techniques. The representative figures herein show the representative numbering.

Analysis of the amino acid sequence of the full-length PRO1007 polypeptide suggests that portions of it possess sequence identity to MAGPIAP, thereby indicating that PRO1007 may be a novel member of the family to which MAGPIAP belongs.

Still analyzing the amino acid sequence of SEQ ID NO:197, the putative signal peptide is at about amino acids 1-30 of SEQ ID NO:197. The transmembrane domain is at amino acids 325-346 of SEQ ID NO:197. N-glycosylation sites are at about amino acids 118-121, 129-132, 163-166, 176-179, 183-186 and

227-130 of SEQ ID NO:197. Ly-6/u-Par domain protein homology is at about amino acids 17-36 and 209-222 of SEQ ID NO:197. The corresponding nucleotides of the amino acids presented herein can be routinely determined given the sequences provided herein.

**EXAMPLE 53: Isolation of cDNA clones Encoding Human PRO1056**

5           Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated herein as 6425. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2  
10           (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55736.

15           In light of an observed sequence homology between the DNA55736 consensus sequence and an EST sequence encompassed within the Merck EST clone no. R88049, the Merck EST clone R88049 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 126 and is herein designated as DNA57693-1424.

20           Clone DNA57693-1424 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 56-58 and ending at the stop codon at nucleotide positions 416-418 (Figure 126). The predicted polypeptide precursor is 120 amino acids long (Figure 127). The full-length PRO1056 protein shown in Figure 127 has an estimated molecular weight of about 13,345 daltons and a pI of about 5.18. Analysis of the full-length PRO1056 sequence shown in Figure 127 (SEQ ID NO:199) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 18, a transmembrane domain from about amino acid 39 to about amino acid 58, a potential N-glycosylation site from about amino acid 86  
25           to about amino acid 89, protein kinase C phosphorylation sites from about amino acid 36 to about amino acid 38 and from about amino acid 58 to about amino acid 60, a tyrosine kinase phosphorylation site from about amino acid 25 to about amino acid 32 and an amino acid sequence block having homology to channel forming colicin proteins from about amino acid 24 to about amino acid 56. Clone DNA57693-1424 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203008.

30           An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 127 (SEQ ID NO:199), evidenced significant homology between the PRO1056 amino acid sequence and the following Dayhoff sequences: PLM\_HUMAN, A40533, ATNG\_HUMAN, A55571, ATNG\_SHEEP, S31524, GEN13025, RIC\_MOUSE, A48678 and A10871\_1.  
35

**EXAMPLE 54: Isolation of cDNA clones Encoding Human PRO826**

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST

cluster sequence from the Incyte database, designated 47283. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program “phrap” (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56000.

In light of an observed sequence homology between the DNA56000 consensus sequence and an EST sequence encompassed within the Merck EST clone no. W69233, the Merck EST clone W69233 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 128 and is herein designated as DNA57694-1341.

Clone DNA57694-1341 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 13-15 and ending at the stop codon at nucleotide positions 310-312 (Figure 128). The predicted polypeptide precursor is 99 amino acids long (Figure 129). The full-length PRO826 protein shown in Figure 129 has an estimated molecular weight of about 11,050 daltons and a pI of about 7.47. Analysis of the full-length PRO826 sequence shown in Figure 129 (SEQ ID NO:201) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 22, potential N-myristoylation sites from about amino acid 22 to about amino acid 27 and from about amino acid 90 to about amino acid 95 and an amino acid sequence block having homology to peroxidase from about amino acid 16 to about amino acid 48. Clone DNA57694-1341 has been deposited with ATCC on June 22, 1998 and is assigned ATCC deposit no. 203017.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 129 (SEQ ID NO:201), evidenced significant homology between the PRO826 amino acid sequence and the following Dayhoff sequences: CCU12315\_1, SCU96108\_6, CELF39F10\_4 and HELT\_HELHO.

#### EXAMPLE 55: Isolation of cDNA clones Encoding Human PRO819

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 49605. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program “phrap” (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56015.

In light of an observed sequence homology between the DNA56015 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H65785, the Merck EST clone H65785 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 130 and is herein designated as DNA57695-1340.

Clone DNA57695-1340 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 46-48 and ending at the stop codon at nucleotide positions 202-204 (Figure 130). The predicted polypeptide precursor is 52 amino acids long (Figure 131). The full-length PRO819 protein shown in Figure 131 has an estimated molecular weight of about 5,216 daltons and a pI of about 4.67. Analysis of the full-length PRO819 sequence shown in Figure 131 (SEQ ID NO:203) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 24, a potential N-myristoylation site from about amino acid 2 to about amino acid 7 and a region having homology to immunoglobulin light chain from about amino acid 5 to about amino acid 33. Clone DNA57695-1340 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203006.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 131 (SEQ ID NO:203), evidenced significant homology between the PRO819 amino acid sequence and the following Dayhoff sequences: HSU03899\_1, HUMIGLITEB\_1, VG28\_HSVSA, AF031522\_1, PAD1\_YEAST and AF045484\_1.

#### EXAMPLE 56: Isolation of cDNA Clones Encoding Human PRO1006

An initial candidate sequence from Incyte cluster sequence no. 45748 was identified using the signal algorithm process described in Example 3 above. This sequence was then aligned with a variety of public and Incyte EST sequences and a consensus sequence designated herein as DNA56036 was derived therefrom.

In light of an observed sequence homology between the DNA56036 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 489737, the Merck EST clone 489737 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 132.

The entire nucleotide sequence of DNA57699-1412 is shown in Figure 132 (SEQ ID NO:204). Clone DNA57699-1412 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 28-30 and ending at the stop codon at nucleotide positions 1204-1206 (Figure 132). The predicted polypeptide precursor is 392 amino acids long (Figure 133). The full-length PRO1006 protein shown in Figure 133 has an estimated molecular weight of about 46,189 daltons and a pI of about 9.04. Clone DNA57699-1412 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:205, the putative signal peptide is at about amino acids 1-23 of SEQ ID NO:205. The N-glycosylation sites are at about amino acids 40-43, 53-56, 204-207 and 373-376 of SEQ ID NO:205. An N-myristoylation site is at about amino acids 273-278 of SEQ ID NO:205.

The corresponding nucleotides of these amino acid regions and others can be routinely determined given the sequences provided herein.

**EXAMPLE 57: Isolation of cDNA Clones Encoding Human PRO1112**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a specific EST cluster sequence. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56018.

In light of an observed sequence homology between the DNA56018 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA223546, the Merck EST clone AA223546 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 134 and is herein designated as DNA57702-1476.

The entire nucleotide sequence of DNA57702-1476 is shown in Figure 134 (SEQ ID NO:206). Clone DNA57702-1476 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 20-22 and ending at the stop codon at nucleotide positions 806-808 of SEQ ID NO:206 (Figure 134). The predicted polypeptide precursor is 262 amino acids long (Figure 135). The full-length PRO1112 protein shown in Figure 135 has an estimated molecular weight of about 29,379 daltons and a pI of about 8.93. Figure 135 also shows the approximate locations of the signal peptide and transmembrane domains. Clone DNA57702-1476 has been deposited with the ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO1112 polypeptide suggests that it possesses some sequence similarity to other proteins. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some sequence identity between the PRO1112 amino acid sequence and at least the following Dayhoff sequences, MTY20B11\_13 (a mycobacterium tuberculosis peptide), F64471, AE000690\_6, XLU16364\_1, E43259 (H<sup>+</sup>-transporting ATP synthase) and PIGSLADRXE\_1 (MHC class II histocompatibility antigen).

**EXAMPLE 58: Isolation of cDNA clones Encoding Human PRO1074**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence (Incyte cluster sequence No. 42586). This cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70

(or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56251.

In light of an observed sequence homology between the DNA56251 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA081912, the Merck EST clone AA081912 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 136 and is the full-length DNA sequence for PRO1074. Clone DNA57704-1452 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209953.

The entire nucleotide sequence of DNA57704-1452 is shown in Figure 136 (SEQ ID NO:208). Clone DNA57704-1452 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 322-324 and ending at the stop codon at nucleotide positions 1315-1317 (Figure 136). The predicted polypeptide precursor is 331 amino acids long (Figure 137). The full-length PRO1074 protein shown in Figure 137 has an estimated molecular weight of about 39,512 Daltons and a pI of about 8.03. Analysis of the full-length PRO1074 sequence shown in Figure 137 (SEQ ID NO:209) evidences the presence of the following features: a transmembrane domain at about amino acids 20 to 39; potential N-glycosylation sites at about amino acids 72 to 75, 154 to 157, 198 to 201, 212 to 215, and 326 to 329; a glycosaminoglycan attachment site at about amino acids 239 to 242, and a Ly-6/u-PAR domain at about amino acids 23 to 36.

Analysis of the amino acid sequence of the full-length PRO1074 polypeptide suggests that it possesses significant sequence similarity to beta 1,3-galactosyltransferase, thereby indicating that PRO1074 may be a novel member of the galactosyltransferase family of proteins. Analysis of the amino acid sequence of the full-length PRO1074 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1074 amino acid sequence and the following Dayhoff sequences: AF029792\_1, P\_R57433, DMU41449\_1, AC000348\_14, P\_R47479, CET09F5\_2, CEF14B6\_4, CET15D6\_5, CEC54C8\_4, and CEE03H4\_10.

Clone DNA57704-1452 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209953.

#### EXAMPLE 59: Isolation of cDNA clones Encoding Human PRO1005

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, Incyte cluster sequence no. 49243. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated



DNA56380.

In light of an observed sequence homology between the DNA56380 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA256657, the Merck EST clone AA256657 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 138 and is herein designated as DNA57708-1411.

The full length clone shown in Figure 138 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 30-32 and ending at the stop codon found at nucleotide positions 585-587 (Figure 138; SEQ ID NO:210). The predicted polypeptide precursor (Figure 139, SEQ ID NO:211) is 185 amino acids long. PRO1005 has a calculated molecular weight of approximately 20,331 daltons and an estimated pI of approximately 5.85. Clone DNA57708-1411 was deposited with the ATCC June 23, 1998, and is assigned ATCC deposit no. 203021.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 139 (SEQ ID NO:211), evidenced some homology between the PRO1005 amino acid sequence and the following Dayhoff sequences: DDU07187\_1, DDU87912\_1, CELD1007\_14, A42239, DDU42597\_1, CYAG\_DICDI, S50452, MRKC\_KLEPN, P-R41998, and XYNA\_RUMFL.

#### EXAMPLE 60: Isolation of cDNA clones Encoding Human PRO1073

An initial DNA sequence referred to herein as DNA55938 and shown in Figure 142 (SEQ ID NO:214) was identified using a yeast screen, in a human SK-Lu-1 adenocarcinoma cell line cDNA library that preferentially represents the 5' ends of the primary cDNA clones. DNA55938 was then compared to ESTs from public databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA), using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. The ESTs were clustered and assembled into a consensus DNA sequence using the computer program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained is designated herein as DNA56411.

In light of an observed sequence homology between the DNA56411 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H86027, the Merck EST clone H86027 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 140.

The full length DNA57710-1451 clone shown in Figure 140 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 345-347 and ending at the stop codon found at nucleotide positions 1242-1244 (Figure 140; SEQ ID NO:212). The predicted polypeptide precursor (Figure 141, SEQ ID NO:213) is 299 amino acids long. PRO1073 has a calculated molecular weight of approximately 34,689 daltons and an estimated pI of approximately 11.49. The PRO1073 polypeptide has the following additional features: a signal peptide at about amino acids 1-31, sequence identity to bZIP transcription factor basic domain signature at about amino acids, a potential N-glycosylation site at about amino acids 2-5, and

sequence identity with protamine P1 proteins at about amino acids 158-183.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 141 (SEQ ID NO:213), revealed some sequence identity between the PRO1073 amino acid sequence and the following Dayhoff sequences: MMU37351\_1, ATAC00250510T9J22.10, S59043, ENXNUPR\_1, B47328, SR55\_DROME, S26650, SON\_HUMAN, VIT2\_CHICK, and XLC4SRPRT\_1.

Clone DNA57710-1451 was deposited with the ATCC on July 1, 1998 and is assigned ATCC deposit no. 203048.

EXAMPLE 61: Isolation of cDNA clones Encoding Human PRO1152

A cDNA clone (DNA57711-1501) encoding a native human PRO1152 polypeptide was identified by employing a yeast screen, in a human infant brain cDNA library that preferentially represents the 5' ends of the primary cDNA clones. Specifically, a yeast screen was employed to identify a cDNA designated herein as DNA55807 (SEQ ID NO:217; see Figure 145).

In light of an observed sequence homology between the DNA55807 sequence and an EST sequence encompassed within the Merck EST clone no. R56756, the Merck EST clone R56756 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 143.

The full-length DNA57711-1501 clone shown in Figure 143 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 58-60 and ending at the stop codon at nucleotide positions 1495-1497 (Figure 143). The predicted polypeptide precursor is 479 amino acids long (Figure 144). The full-length PRO1152 protein shown in Figure 144 has an estimated molecular weight of about 53,602 daltons and a pI of about 8.82. Analysis of the full-length PRO1152 sequence shown in Figure 144 (SEQ ID NO:216) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, transmembrane domains from about amino acid 133 to about amino acid 155, from about amino acid 168 to about amino acid 187, from about amino acid 229 to about amino acid 247, from about amino acid 264 to about amino acid 285, from about amino acid 309 to about amino acid 330, from about amino acid 371 to about amino acid 390 and from about amino acid 441 to about amino acid 464, potential N-glycosylation sites from about amino acid 34 to about amino acid 37 and from about amino acid 387 to about amino acid 390 and an amino acid sequence block having homology to a respiratory-chain NADH dehydrogenase subunit from about amino acid 243 to about amino acid 287. Clone DNA57711-1501 has been deposited with ATCC on July 1, 1998 and is assigned ATCC deposit no. 203047.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 144 (SEQ ID NO:216), evidenced significant homology between the PRO1152 amino acid sequence and the following Dayhoff sequences: AF052239\_1, SYNN9CGA\_1, SFCYTB2\_1, GEN12507, P\_R11769, MTV025\_109, C61168, S43171, P\_P61689 and P\_P61696.

**EXAMPLE 62: Isolation of cDNA clones Encoding Human PRO1136**

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 109142. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56039.

In light of an observed sequence homology between the DNA56039 consensus sequence and an EST sequence encompassed within the Merck EST clone no. HSC1NF011, the Merck EST clone HSC1NF011 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 146 and is herein designated as DNA57827-1493.

Clone DNA57827-1493) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 216-218 and ending at the stop codon at nucleotide positions 2112-2114 (Figure 146). The predicted polypeptide precursor is 632 amino acids long (Figure 147). The full-length PRO1136 protein shown in Figure 147 has an estimated molecular weight of about 69,643 daltons and a pI of about 8.5. Analysis of the full-length PRO1136 sequence shown in Figure 147 (SEQ ID NO:219) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15 and potential N-glycosylation sites from about amino acid 108 to about amino acid 111, from about amino acid 157 to about amino acid 160, from about amino acid 289 to about amino acid 292 and from about amino acid 384 to about amino acid 387. Clone DNA57827-1493 has been deposited with ATCC on July 1, 1998 and is assigned ATCC deposit no. 203045.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 147 (SEQ ID NO:219), evidenced significant homology between the PRO1136 amino acid sequence and the following Dayhoff sequences: AF034746\_1, AF034745\_1, MMAF000168\_19, HSMUPP1\_1, AF060539\_1, SP97\_RAT, I38757, MMU93309\_1, CEK01A6\_4 and HSA224747\_1.

**EXAMPLE 63: Isolation of cDNA clones Encoding Human PRO813**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence (Incyte EST cluster sequence no. 45501. The Incyte EST cluster sequence no. 45501 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)).

Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56400.

5 In light of an observed sequence homology between the DNA56400 consensus sequence and an EST sequence encompassed within the Merck EST clone no. T90592, the Merck EST clone T90592 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 148 and is herein designated DNA57834-1339.

10 The full length clone shown in Figure 148 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 109-111 and ending at the stop codon found at nucleotide positions 637-639 (Figure 149; SEQ ID NO:221). The predicted polypeptide precursor is 176 amino acids long, has a calculated molecular weight of approximately 19,616 daltons and an estimated pI of approximately 7.11. Analysis of the full-length PRO813 sequence shown in Figure 149 (SEQ ID NO:221) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 26 and potential N-myristoylation sites from about amino acid 48 to about amino acid 53, from about amino acid 153 to about  
15 amino acid 158, from about amino acid 156 to about amino acid 161 and from about amino acid 167 to about amino acid 172. Clone DNA57834-1339 has been deposited with the ATCC on June 9, 1998 and is assigned ATCC deposit no. 209954.

20 Analysis of the amino acid sequence of the full-length PRO813 polypeptide suggests that it possesses sequence similarity to the pulmonary surfactant-associated protein C. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO813 amino acid sequence and the following Dayhoff sequences, PSPC\_MUSVI, P\_P92071, G02964, P\_R65489, P\_P82977, P\_R84555, S55542, MUSIGHAJ\_1 and PH1158.

#### EXAMPLE 64: Isolation of cDNA Clones Encoding Human PRO809

25 Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence. The Incyte EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods  
30 in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56418.

35 In light of an observed sequence homology between the DNA56418 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H74302, the Merck EST clone H74302 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 150 and is herein designated DNA57836-1338.

The entire nucleotide sequence of DNA57836-1338 is shown in Figure 150 (SEQ ID NO:222). Clone DNA57836-1338 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 63-65 and ending at the stop codon at nucleotide positions 858-860 of SEQ ID NO:222 (Figure 150). The predicted polypeptide precursor is 265 amino acids long (Figure 151). The full-length PRO809 protein shown in Figure 151 has an estimated molecular weight of about 29,061 daltons and a pI of about 9.18. Figure 151 further shows the approximate positions of the signal peptide and N-glycosylation sites. The corresponding nucleotides can be determined by referencing Figure 150. Clone DNA57836-1338 has been deposited with ATCC on June 23, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO809 polypeptide suggests that it possesses some sequence similarity to the heparin sulfate proteoglycan and to endothelial cell adhesion molecule-1. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO809 amino acid sequence and the following Dayhoff sequences, PGBM\_MOUSE, D82082\_1 and PW14158.

#### EXAMPLE 65: Isolation of cDNA Clones Encoding Human PRO791

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence. The Incyte EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56429.

In light of an observed sequence homology between the DNA56429 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 36367, the Merck EST clone 36367 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 152 and is herein designated DNA57838-1337.

The entire nucleotide sequence of DNA57838-1337 is shown in Figure 152 (SEQ ID NO:224). Clone DNA57838-1337 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 9-11 and ending at the stop codon at nucleotide positions 747-749 of SEQ ID NO:224 (Figure 152). The predicted polypeptide precursor is 246 amino acids long (Figure 153). The full-length PRO791 protein shown in Figure 153 has an estimated molecular weight of about 27,368 daltons and a pI of about 7.45. Figure 153 also shows the approximate locations of the signal peptide, the transmembrane domain, N-glycosylation sites and a region conserved in extracellular proteins. The corresponding nucleotides of one embodiment provided herein can be identified by referencing Figure 152. Clone DNA57838-1337 has been deposited with ATCC on June 23, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and

that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO791 polypeptide suggests that it has sequence similarity with MHC-I antigens, thereby indicating that PRO791 may be related to MHC-I antigens. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some sequence identity between the PRO791 amino acid sequence and the following Dayhoff sequences, AF034346\_1, MMQ1K5\_1 and HFE\_HUMAN.

EXAMPLE 66: Isolation of cDNA clones Encoding Human PRO1004

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence, Incyte cluster sequence No. 73681. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated as DNA56516.

In light of an observed sequence homology between the DNA56516 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H43837, the Merck EST clone H43837 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 154.

The full length clone shown in Figure 154 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 119-121 and ending at the stop codon at nucleotide positions 464-466 (Figure 154; SEQ ID NO:226). The predicted polypeptide precursor is 115 amino acids long (Figure 155; SEQ ID NO:227). The full-length PRO1004 protein shown in Figure 155 has an estimated molecular weight of about 13,649 daltons and a pI of about 9.58. Analysis of the full-length PRO1004 sequence shown in Figure 155 (SEQ ID NO:227) evidences the presence of the following features: a signal peptide at about amino acids 1-24, a microbodies C-terminal targeting signal at about amino acids 113-115, a potential N-glycosylation site at about amino acids 71-74, and a domain having sequence identity with dihydrofolate reductase proteins at about amino acids 22-48.

Analysis of the amino acid sequence of the full-length PRO1004 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1004 amino acid sequence and the following Dayhoff sequences: CELR02D3\_7, LECI\_MOUSE, AF006691\_3, SSZ97390\_1, SSZ97395\_1, and SSZ97400\_1.

Clone DNA57844-1410 was deposited with the ATCC on June 23, 1998, and is assigned ATCC deposit no. 203010.

**EXAMPLE 67: Isolation of cDNA clones Encoding Human PRO1111**

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which had homology to insulin-like growth factor binding protein.

RNA for construction of cDNA libraries was isolated from human fetal brain. The cDNA libraries used to isolate the cDNA clones encoding human PRO1111 were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI.

The human fetal brain cDNA libraries (prepared as described above), were screened by hybridization with a synthetic oligonucleotide probe based upon the Incyte EST sequence described above:

5'-CCACCACCTGGAGGTCCTGCAGTTGGGCAGGAAGTCCATCCGGCAGATTG-3' (SEQ ID NO:251).

An identified cDNA clone was sequenced in entirety. The entire nucleotide sequence of PRO1111 is shown in Figure 156 (SEQ ID NO:228). Clone DNA58721-1475 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 57-59 and a stop codon at nucleotide positions 2016-2018 (Figure 156; SEQ ID NO:228). The predicted polypeptide precursor is 653 amino acids long (Figure 157). The transmembrane domains are at positions 21-40 (type II) and 528-548. Clone DNA58721-1475 has been deposited with ATCC and is assigned ATCC deposit no. 203110. The full-length PRO1111 protein shown in Figure 157 has an estimated molecular weight of about 72,717 daltons and a pI of about 6.99.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 157 (SEQ ID NO:229), revealed some sequence identity between the PRO1111 amino acid sequence and the following Dayhoff sequences: A58532, D86983\_1, RNPLGPV\_1, PGS2\_HUMAN, AF038127\_1, ALS\_MOUSE, GPV\_HUMAN, PGS2\_BOVIN, ALS\_PAPPA and I47020.

**EXAMPLE 68: Isolation of cDNA clones Encoding Human PRO1344**

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA33790. Based on the DNA33790 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1344.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-AGGTTTCGTGATGGAGACAACCGCG-3' (SEQ ID NO:232)

reverse PCR primer 5'-TGTCAAGGACGCACTGCCGTCATG-3' (SEQ ID NO:233)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA33790 sequence which had the following nucleotide sequence

hybridization probe

5'-TGGCCAGATCATCAAGCGTGTCTGTGGCAACGAGCGGCCAGCTCCTATCC-3' (SEQ ID NO:234)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1344 gene using the probe oligonucleotide and one of the PCR primers.

5 RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1344 (designated herein as DNA58723-1588 [Figure 158, SEQ ID NO:230]); and the derived protein sequence for PRO1344.

10 The entire nucleotide sequence of DNA58723-1588 is shown in Figure 158 (SEQ ID NO:230). Clone DNA58723-1588 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 26-28 and ending at the stop codon at nucleotide positions 2186-2188 (Figure 158). The predicted polypeptide precursor is 720 amino acids long (Figure 159). The full-length PRO1344 protein shown in Figure 159 has an estimated molecular weight of about 80,199 daltons and a pI of about 7.77. Analysis of the full-length PRO1344 sequence shown in Figure 159 (SEQ ID NO:231) evidences the presence of the following:  
15 a signal peptide from about amino acid 1 to about amino acid 23, an EGF-like domain cysteine protein signature sequence from about amino acid 260 to about amino acid 271, potential N-glycosylation sites from about amino acid 96 to about amino acid 99, from about amino acid 279 to about amino acid 282, from about amino acid 316 to about amino acid 319, from about amino acid 451 to about amino acid 454 and from about amino acid 614 to about amino acid 617, an amino acid sequence block having homology to serine proteases,  
20 trypsin family from about amino acid 489 to about amino acid 505 and a CUB domain protein profile sequence from about amino acid 150 to about amino acid 166. Clone DNA58723-1588 has been deposited with ATCC on August 18, 1998 and is assigned ATCC deposit no. 203133.

25 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 159 (SEQ ID NO:231), evidenced significant homology between the PRO1344 amino acid sequence and the following Dayhoff sequences: S77063\_1, CRAR\_MOUSE, P\_R74775, P\_P90070, P\_R09217, P\_P70475, HSBMP16\_1 and U50330\_1.

EXAMPLE 69: Isolation of cDNA clones Encoding Human PRO1109

30 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA52642. The consensus DNA sequence was obtained by extending using repeated cycles of BLAST and phrap a previously obtained consensus sequence as far as possible using the sources of EST sequences discussed above. Based on the DNA52642 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence  
35 for PRO1109.



PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CCTTACCTCAGAGGCCAGAGCAAGC-3' (SEQ ID NO:237)

reverse PCR primer 5'-GAGCTTCATCCGTTCTGCGTTCACC-3' (SEQ ID NO:238)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA52642 sequence which had the following nucleotide sequence

hybridization probe

5'-CAGGAATGTAAAGCTTTACAGAGGGTCGCCATCCTCGTTCCCCACC-3' (SEQ ID NO:239)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1109 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human SK-Lu-1 adenocarcinoma cell tissue (LIB247).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1109 (designated herein as DNA58737-1473 [Figure 160, SEQ ID NO:235]) and the derived protein sequence for PRO1109.

The entire nucleotide sequence of DNA58737-1473 is shown in Figure 160 (SEQ ID NO:235). Clone DNA58737-1473 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 119-120 and ending at the stop codon at nucleotide positions 1151-1153 (Figure 160). The predicted polypeptide precursor is 344 amino acids long (Figure 161). The full-length PRO1109 protein shown in Figure 161 has an estimated molecular weight of about 40,041 daltons and a pI of about 9.34. Analysis of the full-length PRO1109 sequence shown in Figure 161 (SEQ ID NO:236) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 27, potential N-glycosylation sites from about amino acid 4 to about amino acid 7, from about amino acid 220 to about amino acid 223 and from about amino acid 335 to about amino acid 338 and an amino acid sequence block having homology to xylose isomerase proteins from about amino acid 191 to about amino acid 201. Clone DNA58737-1473 has been deposited with ATCC on August 18, 1998 and is assigned ATCC deposit no. 203136.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 161 (SEQ ID NO:236), evidenced significant homology between the PRO1109 amino acid sequence and the following Dayhoff sequences: HSUDPGAL\_1, HSUDPB14\_1, NALS\_BOVIN, HSU10473\_1, CEW02B12\_11, YNJ4\_CAEEL, AE000738\_11, CET24D1\_1, S48121 and CEGLY9\_1.

#### EXAMPLE 70: Isolation of cDNA clones Encoding Human PRO1383

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA53961. Based on the DNA53961 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1383.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CATTTTCCTTACCCTGGACCCAGCTCC-3' (SEQ ID NO:242)

reverse PCR primer 5'-GAAAGGCCACAGCACATCTGGCAG-3' (SEQ ID NO:243)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA53961 sequence which had the following nucleotide sequence

hybridization probe

5'-CCACGACCCGAGCAACTTCCTCAAGACCGACTTGTTTCTCTACAGC-3' (SEQ ID NO:244)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1383 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal brain tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1383 (designated herein as DNA58743-1609 [Figure 162, SEQ ID NO: 240]) and the derived protein sequence for PRO1383.

The entire nucleotide sequence of DNA58743-1609 is shown in Figure 162 (SEQ ID NO:240). Clone DNA58743-1609 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 122-124 and ending at the stop codon at nucleotide positions 1391-1393 (Figure 162). The predicted polypeptide precursor is 423 amino acids long (Figure 163). The full-length PRO1383 protein shown in Figure 163 has an estimated molecular weight of about 46,989 daltons and a pI of about 6.77. Analysis of the full-length PRO1383 sequence shown in Figure 163 (SEQ ID NO:241) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 24, a transmembrane domain from about amino acid 339 to about amino acid 362, and potential N-glycosylation sites from about amino acid 34 to about amino acid 37, from about amino acid 58 to about amino acid 61, from about amino acid 142 to about amino acid 145, from about amino acid 197 to about amino acid 200, from about amino acid 300 to about amino acid 303 and from about amino acid 364 to about amino acid 367. Clone DNA58743-1609 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203154.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 163 (SEQ ID NO:241), evidenced significant homology between the PRO1383 amino acid sequence and the following Dayhoff sequences: NMB\_HUMAN, QNR\_COTJA, P\_W38335, P115\_CHICK, P\_W38164, A45993\_1, MMU70209\_1, D83704\_1 and P\_W39176.

#### EXAMPLE 71: Isolation of cDNA Clones Encoding Human PRO1003

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence designated herein as 43055. This sequence was then compared to a variety of EST databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater

that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated consen01.

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2849382, the Incyte EST clone 2849382 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 164.

The entire nucleotide sequence of DNA58846-1409 is shown in Figure 164 (SEQ ID NO:245). Clone DNA58846-1409 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 41-43 and ending at the stop codon at nucleotide positions 293-295 (Figure 164). The predicted polypeptide precursor is 84 amino acids long (Figure 165). The full-length PRO1003 protein shown in Figure 165 has an estimated molecular weight of about 9,408 daltons and a pI of about 9.28. Analysis of the full-length PRO1003 sequence shown in Figure 165 (SEQ ID NO:246) evidences the presence of a signal peptide at amino acids 1 to about 24, and a cAMP- and cGMP-dependent protein kinase phosphorylation site at about amino acids 58 to about 61. Analysis of the amino acid sequence of the full-length PRO1003 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1003 amino acid sequence and the following Dayhoff sequences: AOPCZA363\_3, SRTX\_ATREN, A48298, MHVJHMS\_1, VGL2\_CVMJH, DHDHTC2\_2, CORT\_RAT, TAL6\_HUMAN, P\_W14123, and DVUFI\_2.

#### EXAMPLE 72: Isolation of cDNA Clones Encoding Human PRO1108

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA53237.

In light of an observed sequence homology between the DNA53237 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2379881, the Incyte EST clone 2379881 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 166 and is herein designated DNA58848-1472.

The entire nucleotide sequence of DNA58848-1472 is shown in Figure 166 (SEQ ID NO:247). Clone DNA58848-1472 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 77-79 and ending at the stop codon at nucleotide positions 1445-1447 (Figure 166). The predicted polypeptide precursor is 456 amino acids long (Figure 167). The full-length PRO1108 protein shown in Figure 167 has an estimated molecular weight of about 52,071 daltons and a pI of about 9.46. Analysis of the full-length PRO1108 sequence shown in Figure 167 (SEQ ID NO:248) evidences the presence of the following: type II transmembrane domains from about amino acid 22 to about amino acid 42, from about amino acid 156 to about amino acid 176, from about amino acid 180 to about amino acid 199 and from about amino acid 369 to about amino acid 388, potential N-glycosylation sites from about amino acid 247 to about amino acid 250, from about amino acid 327 to about amino acid 330, from about amino acid 328 to about amino acid 331 and from about amino acid 362 to about amino acid 365 and an amino acid block having homology to ER lumen protein retaining receptor protein from about amino acid 153 to about amino acid 190. Clone DNA58848-1472 has

been deposited with ATCC on June 9, 1998 and is assigned ATCC deposit no. 209955.

Analysis of the amino acid sequence of the full-length PRO1108 polypeptide suggests that it possesses significant sequence similarity to the LPAAT protein, thereby indicating that PRO1108 may be a novel LPAAT homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO1108 amino acid sequence and the following Dayhoff sequences, AF015811\_1, CER07E3\_2, YL35\_CAEEL, S73863, CEF59F4\_4, P\_W06422, MMU41736\_1, MTV008\_39, P\_R99248 and Y67\_BPT7.

#### EXAMPLE 73: Isolation of cDNA Clones Encoding Human PRO1137

The extracellular domain (ECD) sequences (including the secretion signal, if any) of from about 950 known secreted proteins from the Swiss-Prot public protein database were used to search expressed sequence tag (EST) databases. The EST databases included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequence. Using this procedure, Incyte EST No. 3459449, also referred to herein as "DNA7108", was identified as an EST having a BLAST score of 70 or greater that did not encode a known protein.

A consensus DNA sequence was assembled relative to the DNA7108 sequence and other ESTs using repeated cycles of BLAST and the program "phrap" (Phil Green, Univ. of Washington, Seattle, WA). The consensus sequence obtained therefrom is referred to herein as DNA53952.

In light of an observed sequence homology between the DNA53952 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3663102, the Incyte EST clone 3663102 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 168.

The entire nucleotide sequence of DNA58849-1494 is shown in Figure 168 (SEQ ID NO:249). Clone DNA58849-1494 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 77-79 and ending at the stop codon at nucleotide positions 797-799 (Figure 168). The predicted polypeptide precursor is 240 amino acids long (Figure 169). The full-length PRO1137 protein shown in Figure 169 has an estimated molecular weight of about 26,064 daltons and a pI of about 8.65. Analysis of the full-length PRO1137 sequence shown in Figure 169 (SEQ ID NO:250) evidences the presence of a signal peptide at about amino acids 1 to 14 and a potential N-glycosylation site at about amino acids 101-105.

Analysis of the amino acid sequence of the full-length PRO1137 polypeptide suggests that it possesses significant sequence similarity to ribosyltransferase thereby indicating that PRO1137 may be a novel member of the ribosyltransferase family of proteins. Analysis of the amino acid sequence of the full-length PRO1137 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1137 amino acid sequence and the following Dayhoff sequences: MMART5\_1, NARG\_MOUSE, GEN11909, GEN13794, GEN14406, MMRNART62\_1, and P\_R41876.

**EXAMPLE 74: Isolation of cDNA clones Encoding Human PRO1138**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence, Incyte cluster sequence no. 165212. This cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated as DNA54224. The assembly included a proprietary Genentech EST designated herein as DNA49140 (Figure 172; SEQ ID NO:254).

In light of an observed sequence homology between the DNA54224 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3836613, the Incyte EST clone 3836613 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 170 and is the full-length DNA sequence for PRO1138. Clone DNA58850-1495 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209956.

The entire nucleotide sequence of DNA58850-1495 is shown in Figure 170 (SEQ ID NO:252). Clone DNA58850-1495 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 38-40 and ending at the stop codon at nucleotide positions 1043-1045 (Figure 170). The predicted polypeptide precursor is 335 amino acids long (Figure 171). The full-length PRO1138 protein shown in Figure 171 has an estimated molecular weight of about 37,421 Daltons and a pI of about 6.36. Analysis of the full-length PRO1138 sequence shown in Figure 171 (SEQ ID NO:253) evidences the presence of the following features: a signal peptide at about amino acid 1 to about amino acid 22; a transmembrane domain at about amino acids 224 to about 250; a leucine zipper pattern at about amino acids 229 to about 250; and potential N-glycosylation sites at about amino acids 98-101, 142-145, 148-151, 172-175, 176-179, 204-207, and 291-295.

Analysis of the amino acid sequence of the full-length PRO1138 polypeptide suggests that it possesses significant sequence similarity to the CD84, thereby indicating that PRO1138 may be a novel member of the Ig superfamily of polypeptides. More particularly, analysis of the amino acid sequence of the full-length PRO1138 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1138 amino acid sequence and the following Dayhoff sequences: HSU82988\_1, HUMLY9\_1, P\_R97631, P\_R97628, P\_R97629, P\_R97630, CD48\_RAT, CD2\_HUMAN, P\_P93996, and HUMBGP\_1.

Clone DNA58850-1495 was deposited with ATCC on June 9, 1998, and is assigned ATCC deposit no. 209956.

**EXAMPLE 75: Isolation of cDNA clones Encoding Human PRO1054**

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST

cluster sequence from the Incyte database, designated 66212. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program “phrap” (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55722.

In light of an observed sequence homology between the DNA55722 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 319751, the Incyte EST clone 319751 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 173 and is herein designated as DNA58853-1423.

Clone DNA58853-1423 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 46-48 and ending at the stop codon at nucleotide positions 586-588 (Figure 173). The predicted polypeptide precursor is 180 amino acids long (Figure 174). The full-length PRO1054 protein shown in Figure 174 has an estimated molecular weight of about 20,638 daltons and a pI of about 5.0. Analysis of the full-length PRO1054 sequence shown in Figure 174 (SEQ ID NO:256) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 18, a leucine zipper pattern from about amino acid 155 to about amino acid 176 and amino acid sequence blocks having homology to lipocalin proteins from about amino acid 27 to about amino acid 38 and from about amino acid 110 to about amino acid 120. Clone DNA58853-1423 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203016.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 174 (SEQ ID NO:256), evidenced significant homology between the PRO1054 amino acid sequence and the following Dayhoff sequences: MUP1\_MOUSE, MUP6\_MOUSE, MUP2\_MOUSE, MUP8\_MOUSE, MUP5\_MOUSE, MUP4\_MOUSE, S10124, MUPM\_MOUSE, MUP\_RAT and ECU70823\_1.

#### EXAMPLE 76: Isolation of cDNA clones Encoding Human PRO994

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 157555. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program “phrap” (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55728.

In light of an observed sequence homology between the DNA55728 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2860366, the Incyte EST clone 2860366 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 175 and is herein designated as DNA58855-1422.

Clone DNA58855-1422 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 31-33 and ending at the stop codon at nucleotide positions 718-720 (Figure 175). The predicted polypeptide precursor is 229 amino acids long (Figure 176). The full-length PRO994 protein shown in Figure 176 has an estimated molecular weight of about 25,109 daltons and a pI of about 6.83. Analysis of the full-length PRO994 sequence shown in Figure 176 (SEQ ID NO:258) evidences the presence of the following: transmembrane domains from about amino acid 10 to about amino acid 31, from about amino acid 50 to about amino acid 72, from about amino acid 87 to about amino acid 110 and from about amino acid 191 to about amino acid 213, potential N-glycosylation sites from about amino acid 80 to about amino acid 83, from about amino acid 132 to about amino acid 135, from about amino acid 148 to about amino acid 151 and from about amino acid 163 to about amino acid 166 and an amino acid block having homology to TNFR/NGFR cysteine-rich region proteins from about amino acid 4 to about amino acid 11. Clone DNA58855-1422 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203018.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 176 (SEQ ID NO:258), evidenced significant homology between the PRO994 amino acid sequence and the following Dayhoff sequences: AF027204\_1, TAL6\_HUMAN, ILT4\_HUMAN, JC6205, MMU57570\_1, S40363, ETU56093\_1, S42858, P\_R66849 and P\_R74751.

#### EXAMPLE 77: Isolation of cDNA clones Encoding Human PRO812

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 170079. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated as DNA55721.

In light of an observed sequence homology between the DNA55721 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 388964, the Incyte EST clone 388964 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 177 and is herein designated as DNA59205-1421.

Clone DNA59205-1421 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 55-57 and ending at the stop codon at nucleotide positions 304-306 (Figure 177).

The predicted polypeptide precursor is 83 amino acids long (Figure 178). The full-length PRO812 protein shown in Figure 178 has an estimated molecular weight of about 9,201 daltons and a pI of about 9.3. Analysis of the full-length PRO812 sequence shown in Figure 178 (SEQ ID NO:260) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15, a cAMP- and cGMP-dependent protein kinase phosphorylation site from about amino acid 73 to about amino acid 76 and protein kinase C phosphorylation sites from about amino acid 70 to about amino acid 72 and from about amino acid 76 to about amino acid 78. Clone DNA59205-1421 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203009.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 178 (SEQ ID NO:260), evidenced significant homology between the PRO812 amino acid sequence and the following Dayhoff sequences: P\_W35802, P\_W35803, PSC1\_RAT, S68231, GEN13917, PSC2\_RAT, CC10\_HUMAN, UTER\_RABBIT, AF008595\_1 and A56413.

**EXAMPLE 78: Isolation of cDNA clones Encoding Human PRO1069**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence designated herein as 100727. This sequence was then compared to a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56001.

In light of an observed sequence homology between the DNA56001 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3533881, the Incyte EST clone 3533881 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 179 and is the full-length DNA sequence for PRO1069. Clone DNA59211-1450 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209960.

The entire nucleotide sequence of DNA59211-1450 is shown in Figure 179 (SEQ ID NO:261). Clone DNA59211-1450 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 197-199 and ending at the stop codon at nucleotide positions 464-466. The predicted polypeptide precursor is 89 amino acids long (Figure 180). The full-length PRO1069 protein shown in Figure 180 has an estimated molecular weight of about 9,433 daltons and a pI of about 8.21. Analysis of the full-length PRO1069 sequence shown in Figure 180 (SEQ ID NO:262) evidences the presence of the following features: a signal peptide sequence at amino acid 1 to about 16; a transmembrane domain at about amino acids 36 to about 59; potential N-myristoylation sites at about amino acids 41-46, 45-50, and 84-89; and homology with extracellular proteins SCP/Tpx-1/Ag5/PR-1/Sc7 at about amino acids 54 to about 66.



Analysis of the amino acid sequence of the full-length PRO1069 polypeptide suggests that it possesses significant sequence similarity to CHIF, thereby indicating that PRO1069 may be a member of the CHIF family of polypeptides. More particularly, analysis of the amino acid sequence of the full-length PRO1069 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1069 amino acid sequence and the following Dayhoff sequences: CHIF\_RAT, A55571, PLM\_HUMAN, A40533, ATNG\_BOVIN, RIC\_MOUSE, PETD\_SYNY3, VTB1\_XENLA, A05009, and S75086.

Clone DNA59211-1450 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209960.

**EXAMPLE 79: Isolation of cDNA Clones Encoding Human PRO1129**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence designated herein as 98833. The Incyte EST cluster sequence no. 98833 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56038.

In light of an observed sequence homology between the DNA56038 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1335241, the Incyte EST clone 1335241 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 181 and is herein designated DNA59213-1487.

The full length clone shown in Figure 181 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 42-44 and ending at the stop codon found at nucleotide positions 1614-1616 (Figure 181; SEQ ID NO:263). The predicted polypeptide precursor is 524 amino acids long, has a calculated molecular weight of approximately 60,310 daltons and an estimated pI of approximately 7.46. Analysis of the full-length PRO1129 sequence shown in Figure 182 (SEQ ID NO:264) evidences the presence of the following: type II transmembrane domains from about amino acid 13 to about amino acid 32 and from about amino acid 77 to about amino acid 102, a cytochrome P-450 cysteine heme-iron ligand signature sequence from about amino acid 461 to about amino acid 470 and potential N-glycosylation sites from about amino acid 112 to about amino acid 115 and from about amino acid 168 to about amino acid 171. Clone DNA59213-1487 has been deposited with the ATCC on June 9, 1998 and is assigned ATCC deposit no. 209959.

Analysis of the amino acid sequence of the full-length PRO1129 polypeptide suggests that it possesses sequence similarity to the cytochrome P-450 family of proteins. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO1129 amino acid

sequence and the following Dayhoff sequences, AC004523\_1, S45702, AF054821\_1 and I53015.

**EXAMPLE 80: Isolation of cDNA clones Encoding Human PRO1068**

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated Incyte cluster no. 141736. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. One or more of the ESTs was derived from a human mast cell line from a patient with mast cell leukemia. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56094.

In light of an observed sequence homology between the DNA56094 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 004974, the Incyte EST clone 004974 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 183 and is herein designated as DNA59214-1449 (SEQ ID NO:265).

The full length clone shown in Figure 183 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 42-44 and ending at the stop codon found at nucleotide positions 414-416 (Figure 183; SEQ ID NO:265). The predicted polypeptide precursor (Figure 184, SEQ ID NO:266) is 124 amino acids long. PRO1068 has a calculated molecular weight of approximately 14,284 daltons and an estimated pI of approximately 8.14. The PRO1068 polypeptide has the following additional features: a signal peptide sequence at about amino acids 1-20, a urotensin II signature sequence at about amino acids 118-123, a cell attachment sequence at about amino acids 64-66, and a potential cAMP- and cGMP-dependent protein kinase phosphorylation site at about amino acids 112-115.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 184 (SEQ ID NO:266), revealed homology between the PRO1068 amino acid sequence and the following Dayhoff sequences: HALBOP\_1, MTV043\_36, I50498, and P\_R78445

Clone DNA59214-1449 was deposited with the ATCC on July 1, 1998 and is assigned ATCC deposit no.203046.

**EXAMPLE 81: Isolation of cDNA clones Encoding Human PRO1066**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence designated herein as 79066. The Incyte EST cluster sequence no. 79066 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST

databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56121.

In light of an observed sequence homology between the DNA56121 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1515315, the Incyte EST clone 1515315 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 185 and is herein designated DNA59215-1425.

The full length clone shown in Figure 185 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 176-178 and ending at the stop codon found at nucleotide positions 527-529 (Figure 185; SEQ ID NO:267). The predicted polypeptide precursor is 117 amino acids long, has a calculated molecular weight of approximately 12,911 daltons and an estimated pI of approximately 5.46. Analysis of the full-length PRO1066 sequence shown in Figure 186 (SEQ ID NO:268) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 23, a cAMP- and cGMP-dependent protein kinase phosphorylation site from about amino acid 38 to about amino acid 41 and potential N-myristoylation sites from about amino acid 5 to about amino acid 10, from about amino acid 63 to about amino acid 68 and from about amino acid 83 to about amino acid 88. Clone UNQ524 (DNA59215-1425) has been deposited with the ATCC on June 9, 1998 and is assigned ATCC deposit no. 209961.

Analysis of the amino acid sequence of the full-length PRO1066 polypeptide suggests that it does not possess significant sequence similarity to any known human protein. However, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO1066 amino acid sequence and the following Dayhoff sequences, MOTI\_HUMAN, AF025667\_1, MTCY19H9\_8 and RABIGKCH\_1.

#### EXAMPLE 82: Isolation of cDNA Clones Encoding Human PRO1184

Use of the signal sequence algorithm described in Example 3 on ESTs from an Incyte database allowed identification a candidate sequence designated herein as DNA56375. This sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56375.

In light of an observed sequence homology between the DNA56375 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1428374, the Incyte EST clone 1428374 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 187.

The full length clone shown in Figure 187 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 106-108 and ending at the stop codon found at nucleotide positions 532-534 (Figure 187; SEQ ID NO:269). The predicted polypeptide precursor is 142 amino acids long, has a calculated molecular weight of approximately 15,690 daltons and an estimated pI of approximately 9.64. Analysis of the full-length PRO1184 sequence shown in Figure 188 (SEQ ID NO:270) evidences the presence of a signal peptide at about amino acids 1-38. Clone DNA59220-1514 has been deposited with the ATCC on June 9, 1998. It is understood that the deposited clone has the actual sequences and that representations are presented herein.

Analysis of the amino acid sequence of the full-length PRO1184 polypeptide suggests that it possesses some sequence identity with a protein called TIM from *Drosophila virilis*, designated "DVTIMS02\_1" in the Dayhoff data base, (version 35.45 SwissProt 35). Other Dayhoff database (version 35.45 SwissProt 35) sequences having some degree of sequence identity with PRO1184 include: WIS1\_SCHPO, F002186\_1, ATAC00239124 and MSAIPRP\_1.

#### EXAMPLE 83: Isolation of cDNA clones Encoding Human PRO1360

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST sequence from an Incyte database, designated DNA10572. This EST sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank, Merck/Wash. U.) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57314.

In light of an observed sequence homology between the DNA57314 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA406443, the Merck EST clone AA406443 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 189 and is herein designated as DNA59488-1603.

The full length clone shown in Figure 189 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 54-56 and ending at the stop codon found at nucleotide positions 909-911 (Figure 189; SEQ ID NO:271). The predicted polypeptide precursor (Figure 190, SEQ ID NO:272) is 285 amino acids long. PRO1360 has a calculated molecular weight of approximately 31,433 daltons and an estimated pI of approximately 7.32. Clone DNA59488-1603 was deposited with the ATCC on

August 25, 1998 and is assigned ATCC deposit no. 203157.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 190 (SEQ ID NO:272), revealed sequence identity between the PRO1360 amino acid sequence and the following Dayhoff sequences: UN51\_CAEEL, YD4B\_SCHPO, AF000634\_1, GFO\_ZYMMO, YE1J\_SCHPO, D86566\_1, ZMGFO\_1, S76976, PPSA\_SYNY3, and CEF28B1\_4.

**EXAMPLE 84: Isolation of cDNA clones Encoding Human PRO1029**

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 18763. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57854.

In light of an observed sequence homology between the DNA57854 consensus sequence and an EST sequence encompassed within the Merck EST clone no. T98880, the Merck EST clone T98880 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 191 and is herein designated as DNA59493-1420.

Clone DNA59493-1420 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 39-41 and ending at the stop codon at nucleotide positions 297-299 (Figure 191). The predicted polypeptide precursor is 86 amino acids long (Figure 192). The full-length PRO1029 protein shown in Figure 192 has an estimated molecular weight of about 9,548 daltons and a pI of about 8.52. Analysis of the full-length PRO1029 sequence shown in Figure 192 (SEQ ID NO:274) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19, an amino acid block having homology to bacterial rhodopsins retinal binding site protein from about amino acid 50 to about amino acid 61, a prenyl group binding site from about amino acid 83 to about amino acid 86 and a potential N-glycosylation site from about amino acid 45 to about amino acid 48. Clone DNA59493-1420 has been deposited with ATCC on July 1, 1998 and is assigned ATCC deposit no. 203050,

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 192 (SEQ ID NO:274), evidenced significant homology between the PRO1029 amino acid sequence and the following Dayhoff sequences: S66088, AF031815\_1, MM4A6L\_1, PSEIS52a-1, S17699 and P\_R63635.

**EXAMPLE 85: Isolation of cDNA clones Encoding Human PRO1139**

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST

cluster sequence from the Incyte database, designated 4461. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57312.

The DNA57312 consensus sequence included a 172 nucleotides long public EST (T62095, Merck/University of Washington public database). This EST clone, identified herein as a putative protein coding sequence, was purchased from Merck, and sequenced to provide the coding sequence of PRO1139 (Figure 193). As noted before, the deduced amino acid sequence of DNA59497-1496 shows a significant sequence identity with the deduced amino acid sequence of HSOBRGRP\_1. The full-length protein (Figure 194) contains a putative signal peptide between amino acid residues 1 and about 28, and three putative transmembrane domains (approximate amino acid residues 33-52, 71-89, 98-120).

#### EXAMPLE 86: Isolation of cDNA clones Encoding Human PRO1309

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed homology to SLIT.

RNA for construction of cDNA libraries was isolated from human fetal brain tissue. The cDNA libraries used to isolate the cDNA clones encoding human PRO1309 were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI.

The cDNA libraries (prepared as described above), were screened by hybridization with a synthetic oligonucleotide probe derived from the above described Incyte EST sequence:

5'-TCCGTGCAGGGGGACGCCTTTCAGAACTGCGCCGAGTTAAGGAAC-3' (SEQ ID NO:279).

A cDNA clone was isolated and sequenced in entirety. The entire nucleotide sequence of DNA59588-1571 is shown in Figure 195 (SEQ ID NO:277). Clone DNA59588-1571 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 720-722 and a stop codon at nucleotide positions 2286-2288 (Figure 195; SEQ ID NO:277). The predicted polypeptide precursor is 522 amino acids long. The signal peptide is approximately at 1-34 and the transmembrane domain is at approximately 428-450 of SEQ ID NO:278. Clone DNA59588-1571 has been deposited with ATCC and is assigned ATCC deposit no. 203106. The full-length PRO1309 protein shown in Figure 196 has an estimated molecular weight of about 58,614 daltons and a pI of about 7.42.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 196 (SEQ ID NO:278), revealed sequence identity between the PRO1309 amino acid sequence and the following Dayhoff sequences: AB007876\_1, GPV\_MOUSE, ALS\_RAT, P\_R85889, LUM\_CHICK, AB014462\_1, PGS1\_CANFA, CEM88\_7, A58532 and GEN11209.

#### EXAMPLE 87: Isolation of cDNA Clones Encoding Human PRO1028

Use of the signal sequence algorithm described in Example 3 above allowed identification of a certain EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA59603.

In light of an observed sequence homology between the DNA59603 sequence and an EST sequence contained within Incyte EST clone no. 1497725, the Incyte EST clone no. 1497725 was purchased and the cDNA insert was obtained and sequenced. It was found that the insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 197 and is herein designated as DNA59603-1419.

The entire nucleotide sequence of DNA59603-1419 is shown in Figure 197 (SEQ ID NO:280). Clone DNA59603-1419 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 21-23 and ending at the stop codon at nucleotide positions 612-614 (Figure 197). The predicted polypeptide precursor is 197 amino acids long (Figure 198). The full-length PRO1028 protein shown in Figure 198 has an estimated molecular weight of about 20,832 daltons and a pI of about 8.74. Clone DNA59603-1419 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:281, the putative signal peptide is at about amino acids 1-19 of SEQ ID NO:281. An N-glycosylation site is at about amino acids 35-38 of SEQ ID NO:281. A C-type lectin domain is at about amino acids 108-117 of SEQ ID NO:281, indicating that PRO513 may be related to or be a lectin. The corresponding nucleotides of these amino acid sequences or others can be routinely determined given the sequences provided herein.

#### EXAMPLE 88: Isolation of cDNA Clones Encoding Human PRO1027

Use of the signal sequence algorithm described in Example 3 above allowed identification of a certain EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing

homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56399.

5 In light of an observed sequence homology between the DNA56399 sequence and an EST sequence contained within Incyte EST clone no. 937605, the Incyte EST clone no. 937605 was purchased and the cDNA insert was obtained and sequenced. It was found that the insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 199 and is herein designated as DNA59605-1418.

10 The entire nucleotide sequence of DNA59605-1418 is shown in Figure 199 (SEQ ID NO:282). Clone DNA59605-1418 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 31-33 and ending at the stop codon at nucleotide positions 262-264 (Figure 199). The predicted polypeptide precursor is 77 amino acids long (Figure 200). The full-length PRO1027 protein shown in Figure 200 has an estimated molecular weight of about 8,772 daltons and a pI of about 9.62. Clone DNA59605-1418 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains  
15 the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:283, the putative signal peptide is at about amino acids 1-33 of SEQ ID NO:283. The type II fibronectin collagen-binding domain begins at about amino acid 30 of SEQ ID NO:283. The corresponding nucleotides for these amino acid sequences and others can be routinely determined given the sequences provided herein. PRO1027 may be involved in tissue formation or  
20 repair.

The following Dayhoff designations appear to have some sequence identity with PRO1027: SFT2\_YEAST; ATM3E9\_2; A69826; YM16\_MARPO; E64896; U60193\_2; MTLRAJ205\_1; MCU60315\_70; SPAS\_SHIFL; and S54213.

#### 25 EXAMPLE 89: Isolation of cDNA Clones Encoding Human PRO1107

Use of the signal sequence algorithm described in Example 3 above allowed identification of a certain EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing  
30 homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56402.

35 In light of an observed sequence homology between the DNA56402 sequence and an EST sequence contained within Incyte EST clone no. 3203694, the Incyte EST clone no. 3203694 was purchased and the cDNA insert was obtained and sequenced. It was found that the insert encoded a full-length protein. The



sequence of this cDNA insert is shown in Figure 201 and is herein designated as DNA59606-1471.

The entire nucleotide sequence of DNA59606-1471 is shown in Figure 201 (SEQ ID NO:284). Clone DNA59606-1471 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 244-246 and ending at the stop codon at nucleotide positions 1675-1677 of SEQ ID NO:284 (Figure 201). The predicted polypeptide precursor is 477 amino acids long (Figure 202). The full-length PRO1107 protein shown in Figure 202 has an estimated molecular weight of about 54,668 daltons and a pI of about 6.33. Clone DNA59606-1471 has been deposited with ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO1107 polypeptide suggests that it possesses significant sequence similarity to phosphodiesterase I/nucleotide pyrophosphatase, human insulin receptor tyrosine kinase inhibitor, alkaline phosphodiesterase and autotaxin, thereby indicating that PRO1107 may have at least one or all of the activities of these proteins, and that PRO1107 is a novel phosphodiesterase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO1107 amino acid sequence and at least the following Dayhoff sequences: AF005632\_1, P\_R79148, RNU78787\_1, AF060218\_4, A57080 and HUMATXT\_1.

#### EXAMPLE 90: Isolation of cDNA clones Encoding Human PRO1140

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence, Incyte cluster sequence No. 135917. This sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56416.

In light of an observed sequence homology between DNA56416 and an EST sequence contained within Incyte EST clone no. 3345705, Incyte EST clone no. 3345705 was obtained and its insert sequenced. It was found that the insert encoded a full-length protein. The sequence, designated herein as DNA59607-1497, which is shown in Figure 203, is the full-length DNA sequence for PRO1140. Clone DNA59607-1497 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209946.

The entire nucleotide sequence of DNA59607-1497 is shown in Figure 203 (SEQ ID NO:286). Clone DNA59607-1497 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 210-212 and ending at the stop codon at nucleotide positions 975-977 (Figure 203). The predicted polypeptide precursor is 255 amino acids long (Figure 204). The full-length PRO1140 protein shown in Figure 204 has an estimated molecular weight of about 29,405 daltons and a pI of about 7.64. Analysis of the full-length PRO1140 sequence shown in Figure 204 (SEQ ID NO:287) evidences the presence of three

transmembrane domains at about amino acids 101 to 118, 141 to 161 and 172 to 191.

Analysis of the amino acid sequence of the full-length PRO1140 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1140 amino acid sequence and the following Dayhoff sequences: AF023602\_1, AF000368\_1, CIN3\_RAT, AF003373\_1, GEN13279, and AF003372\_1.

Clone DNA59607-1497 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209946.

#### EXAMPLE 91: Isolation of cDNA clones Encoding Human PRO1106

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence. This sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56423.

In light of an observed sequence homology between DNA56423 and an EST sequence contained within Incyte EST clone no. 1711247, Incyte EST clone no. 1711247 was obtained and its insert sequenced. It was found that the insert encoded a full-length protein. The sequence, designated herein as DNA59609-1470, which is shown in Figure 205, is the full-length DNA sequence for PRO1106. Clone DNA59609-1470 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209963.

The entire nucleotide sequence of DNA59609-1470 is shown in Figure 205 (SEQ ID NO:288). Clone DNA59609-1470 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 61-63 and ending at the stop codon at nucleotide positions 1468-1470 of SEQ ID NO:288 (Figure 205). The predicted polypeptide precursor is 469 amino acids long (Figure 206). The full-length PRO1106 protein shown in Figure 206 has an estimated molecular weight of about 52,689 daltons and a pI of about 8.68. It is understood that the skilled artisan can construct the polypeptide or nucleic acid encoding therefor to exclude any one or more of all of these domains. For example, the transmembrane domain region(s) and/or either of the amino terminal or carboxyl end can be excluded. Clone DNA59609-1470 has been deposited with ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO1106 polypeptide suggests that it possesses significant sequence similarity to the peroxisomal ca-dependent solute carrier, thereby indicating that PRO1106 may be a novel transporter. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO1106 amino acid sequence and at least the following Dayhoff sequences, AF004161\_1, IG002N01\_25, GDC\_BOVIN and BT1\_MAIZE.

**EXAMPLE 92: Isolation of cDNA clones Encoding Human PRO1291**

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 120480. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56425.

In light of an observed sequence homology between the DNA56425 sequence and an EST sequence encompassed within the Incyte EST clone no. 2798803, the Incyte EST clone 2798803 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 207 and is herein designated as DNA59610-1556.

Clone DNA59610-1556 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 61-63 and ending at the stop codon at nucleotide positions 907-909 (Figure 207). The predicted polypeptide precursor is 282 amino acids long (Figure 208). The full-length PRO1291 protein shown in Figure 208 has an estimated molecular weight of about 30,878 daltons and a pI of about 5.27. Analysis of the full-length PRO1291 sequence shown in Figure 208 (SEQ ID NO:291) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, a transmembrane domain from about amino acid 258 to about amino acid 281 and potential N-glycosylation sites from about amino acid 112 to about amino acid 115, from about amino acid 160 to about amino acid 163, from about amino acid 190 to about amino acid 193, from about amino acid 196 to about amino acid 199, from about amino acid 205 to about amino acid 208, from about amino acid 216 to about amino acid 219 and from about amino acid 220 to about amino acid 223.. Clone DNA59610-1556 has been deposited with ATCC on June 16, 1998 and is assigned ATCC deposit no. 209990.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 208 (SEQ ID NO:291), evidenced significant homology between the PRO1291 amino acid sequence and the following Dayhoff sequences: HSU90552\_1, HSU90144\_1, AF033107\_1, HSB73\_1, HSU90142\_1, GGCD80\_1, P\_W34452, MOG\_MOUSE, B39371 and P\_R71360.

**EXAMPLE 93: Isolation of cDNA clones Encoding Human PRO1105**

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul

et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56430.

In light of an observed sequence homology between the DNA56430 sequence and an EST sequence encompassed within the Incyte EST clone no. 1853047, the Incyte EST clone 1853047 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 209 and is herein designated as DNA59612-1466.

The entire nucleotide sequence of DNA59612-1466 is shown in Figure 209 (SEQ ID NO:292). Clone DNA59612-1466 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 28-30 and ending at the stop codon at nucleotide positions 568-570 of SEQ ID NO:292 (Figure 209). The predicted polypeptide precursor is 180 amino acids long (Figure 210). The full-length PRO1105 protein shown in Figure 210 has an estimated molecular weight of about 20,040 daltons and a pI of about 8.35. Clone DNA59612-1466 has been deposited with the ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analyzing Figure 210, a signal peptide is at about amino acids 1-19 of SEQ ID NO:293 and transmembrane domains are shown at about amino acids 80-99 and 145-162 of SEQ ID NO:293. It is understood that the skilled artisan could form a polypeptide with all of or any combination or individual selection of these regions. It is also understood that the corresponding nucleic acids can be routinely identified and prepared based on the information provided herein.

#### EXAMPLE 94: Isolation of cDNA clones Encoding Human PRO511

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56434.

In light of an observed sequence homology between the DNA56434 sequence and an EST sequence encompassed within the Incyte EST clone no. 1227491, the Incyte EST clone 1227491 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 211 and is herein designated as DNA59613-1417.

The entire nucleotide sequence of DNA59613-1417 is shown in Figure 211 (SEQ ID NO:294). Clone DNA59613-1417 contains a single open reading frame with an apparent translational initiation site at nucleotide

positions 233-235 and ending at the stop codon at nucleotide positions 944-946 (Figure 211). The predicted polypeptide precursor is 237 amino acids long (Figure 212). The full-length PRO511 protein shown in Figure 212 has an estimated molecular weight of about 25,284 daltons and a pI of about 5.74. Clone DNA59613-1417 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

5 Analyzing the amino acid sequence of SEQ ID NO:295, the putative signal peptide is at about amino acids 1-25 of SEQ ID NO:295. The N-glycosylation sites are at about amino acids 45-48, 73-76, 107-110, 118-121, 132-135, 172-175, 175-178 and 185-188 of SEQ ID NO:295. An arthropod defensins conserved region is at about amino acids 176-182 of SEQ ID NO:295. A kringle domain begins at about amino acid 128 of SEQ ID NO:295 and a ly-6/u-PAR domain begins at about amino acid 6 of SEQ ID NO:295. The  
10 corresponding nucleotides of these amino acid sequences and others can be routinely determined given the sequences provided herein.

The designations appearing in a Dayhoff database with which PRO511 has some sequence identity are as follows: SSC20F10\_1; SF041083; P\_W26579; S44208; JC2394; PSTA\_DICDI; A27020; S59310; RAG1\_RABIT; and MUSBALBC1\_1.

#### 15 EXAMPLE 95: Isolation of cDNA clones Encoding Human PRO1104

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a  
20 proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle,  
25 Washington). The consensus sequence obtained therefrom is herein designated DNA56446.

In light of an observed sequence homology between the DNA56446 sequence and an EST sequence encompassed within the Incyte EST clone no. 2837496, the Incyte EST clone 2837496 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 213 and is herein designated as DNA59616-1465.

30 The entire nucleotide sequence of DNA59616-1465 is shown in Figure 213 (SEQ ID NO:296). Clone DNA59616-1465 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 109-111 and ending at the stop codon at nucleotide positions 1132-1134 of SEQ ID NO:296 (Figure 213). The predicted polypeptide precursor is 341 amino acids long (Figure 214). The full-length PRO1104 protein shown in Figure 214 has an estimated molecular weight of about 36,769 daltons and a pI of about 9.03.  
35 Clone DNA59616-1465 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analyzing Figure 214, a signal peptide is at about amino acids 1-22 of SEQ ID NO:297. N-myristoylation sites are at about amino acids 41-46, 110-115, 133-138, 167-172 and 179-184 of SEQ ID NO:297.

**EXAMPLE 96: Isolation of cDNA clones Encoding Human PRO1100**

5 Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

15 In light of an observed sequence homology between the obtained consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2305379, the Incyte EST clone 2305379 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 215 and is herein designated as DNA59619-1464.

20 The entire nucleotide sequence of DNA59619-1464 is shown in Figure 215 (SEQ ID NO:298). Clone DNA59619-1464 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 33-35 and ending at the stop codon at nucleotide positions 993-995 of SEQ ID NO:298 (Figure 215). The predicted polypeptide precursor is 320 amino acids long (Figure 216). The full-length PRO1100 protein shown in Figure 216 has an estimated molecular weight of about 36,475 daltons and a pI of about 7.29. Clone DNA59619-1464 has been deposited with ATCC on July 1, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

25 Upon analyzing SEQ ID NO:299, the approximate locations of the signal peptide, the transmembrane domains, an N-glycosylation site, an N-myristoylation site, a CUB domain and an amiloride-sensitive sodium channel domain are present. It is believed that PRO1100 may function as a channel. The corresponding nucleic acids for these amino acids and others can be routinely determined given SEQ ID NO:299..

**EXAMPLE 97: Isolation of cDNA clones Encoding Human PRO836**

35 Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70

(or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained is herein designated DNA56453.

In light of an observed sequence homology between the DNA56453 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2610075, the Incyte EST clone 2610075 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 217 and is herein designated as DNA59620-1463.

The entire nucleotide sequence of DNA59620-1463 is shown in Figure 217 (SEQ ID NO:300). Clone DNA59620-1463 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 65-67 and ending at the stop codon at nucleotide positions 1448-1450 of SEQ ID NO:300 (Figure 217). The predicted polypeptide precursor is 461 amino acids long (Figure 218). The full-length PRO836 protein shown in Figure 218 has an estimated molecular weight of about 52,085 daltons and a pI of about 5.36. Analysis of the full-length PRO836 sequence shown in Figure 218 (SEQ ID NO:301) evidences the presence of the following: a signal peptide, N-glycosylation sites, N-myristoylation sites, a domain conserved in the YJL126w/YLR351c/yhcX family of proteins, and a region having sequence identity with SLS1. Clone DNA59620-1463 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO836 polypeptide suggests that it possesses some sequence similarity to SLS1, thereby indicating that PRO836 may be involved in protein translocation of the ER. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some homology between the PRO836 amino acid sequence and at least the following Dayhoff sequences, S58132, SPBC3B9\_1, S66714, CRU40057\_1 and IMA\_CAEL.

#### EXAMPLE 98: Isolation of cDNA clones Encoding Human PRO1141

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 11873. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56518.

In light of an observed sequence homology between the DNA56518 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2679995, the Incyte EST clone 2679995 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 219 and is herein designated as DNA59625-1498.

Clone DNA59625-1498 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 204-206 and ending at the stop codon at nucleotide positions 945-947 (Figure 219). The predicted polypeptide precursor is 247 amino acids long (Figure 220). The full-length PRO1141 protein shown in Figure 220 has an estimated molecular weight of about 26,840 daltons and a pI of about 8.19. Analysis of the full-length PRO1141 sequence shown in Figure 220 (SEQ ID NO:303) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19 and transmembrane domains from about amino acid 38 to about amino acid 57, from about amino acid 67 to about amino acid 83, from about amino acid 117 to about amino acid 139 and from about amino acid 153 to about amino acid 170. Clone DNA59625-1498 has been deposited with ATCC on June 16, 1998 and is assigned ATCC deposit no. 209992.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 220 (SEQ ID NO:303), evidenced significant homology between the PRO1141 amino acid sequence and the following Dayhoff sequences: CEVF36H2L\_2, PCRB7PRJ\_1, AB000506\_1, LEU95008\_1, MRU87980\_15, YIGM\_ECOLI, STU65700\_1, GHU62778\_1, CYST\_SYNY3 and AF009567\_1.

#### EXAMPLE 99: Isolation of cDNA clones Encoding Human PRO1132

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein as DNA35934. Based on the DNA35934 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1132.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'-TCCTGTGACCACCCCTCTAACACC-3' (SEQ ID NO:310) and

reverse PCR primer: 5'-CTGGAACATCTGCTGCCCAGATTC-3' (SEQ ID NO:311).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus sequence which had the following nucleotide sequence:

5'-GTCGGATGACAGCAGCAGCCGCATCATCAATGGATCCGACTGCGATATGC-3' (SEQ ID NO:312).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1132 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1132 and the derived protein sequence for PRO1132.

The entire nucleotide sequence of PRO1132 is shown in Figure 225 (SEQ ID NO:308). Clone DNA59767-1489 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 354-356 and a stop codon at nucleotide positions 1233-1235 (Figure 225; SEQ ID NO:308). The predicted polypeptide precursor is 293 amino acids long. The signal peptide is at about amino acids 1-22 and the histidine active site is at about amino acids 104-109 of SEQ ID NO:309. Clone DNA59767-1489 has been



deposited with ATCC (having the actual sequence rather than representations based on sequencing techniques as presented herein) and is assigned ATCC deposit no. 203108. The full-length PRO1132 protein shown in Figure 226 has an estimated molecular weight of about 32,020 daltons and a pI of about 8.7.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 226 (SEQ ID NO:309), revealed sequence identity between the PRO1132 amino acid sequence and the following Dayhoff sequences: SSU76256\_1, P\_W10694, MMAE000663\_6, AF013988\_1, U66061\_8, MMAE000665\_2, MMAE00066415, MMAE00066414, MMAE000665\_4 and MMAE00066412.

#### EXAMPLE 100: Isolation of cDNA clones Encoding Human NL7 (PRO1346)

A single EST sequence (#1398422) was found in the LIFESEQ<sup>®</sup> database as described in Example 1 above. This EST sequence was renamed as DNA45668. Based on the DNA45668 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for NL7.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'-CACACGTCCAACCTCAATGGGCAG-3' (SEQ ID NO:315)

reverse PCR primer: 5'-GACCAGCAGGGCCAAGGACAAGG-3' (SEQ ID NO:316)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA45668 sequence which had the following nucleotide sequence:

hybridization probe:

5'-GTTCTCTGAGATGAAGATCCGGCCGGTCCGGGAGTACCGCTTAG-3'  
(SEQ ID NO:317)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the NL7 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from a human fetal kidney library (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for NL7 (designated herein as DNA59776-1600 [Figure 227, SEQ ID NO:313]) and the derived protein sequence for NL7 (PRO1346).

The entire coding sequence of NL7 (PRO1346) is shown in Figure 227 (SEQ ID NO:313). Clone DNA59776-1600 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 1-3 and an apparent stop codon at nucleotide positions 1384-1386. The predicted polypeptide precursor is 461 amino acids long. The protein contains an apparent type II transmembrane domain at amino acid positions from about 31 to about 50; fibrinogen beta and gamma chains C-terminal domain signature starting at about amino acid position 409, and a leucine zipper pattern starting at about amino acid positions 140, 147, 154 and 161, respectively. Clone DNA59776-1600 has been deposited with ATCC and is assigned ATCC deposit no. 203128. The full-length NL7 protein shown in Figure 228 has an estimated molecular weight of about 50,744 daltons and a pI of about 6.38.

Based on a WU-BLAST2 sequence alignment analysis (using the WU-BLAST2 computer program) of the full-length sequence, NL7 shows significant amino acid sequence identity to a human microfibril-associated glycoprotein (1 MFA4\_HUMAN); to known TIE-2 ligands and ligand homologues, ficolin, serum lectin and TGF-1 binding protein.

#### 5 EXAMPLE 101: Isolation of cDNA clones Encoding Human PRO1131

A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated DNA43546 (see Figure 231; SEQ ID NO:320). The DNA43546 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing  
10 homologues. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA45627.

15 Based on the DNA45627 sequence, oligonucleotide probes were generated and used to screen a human library prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

PCR primers (forward and 2 reverse) were synthesized:

20 forward PCR primer 5'-ATGCAGGCCAAGTACAGCAGCAC-3' (SEQ ID NO:321);  
reverse PCR primer 1 5'-CATGCTGACGACTTCCTGCAAGC-3' (SEQ ID NO:322); and  
reverse PCR primer 1 5'-CCACACAGTCTCTGCTTCTTGGG-3' (SEQ ID NO:323)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA45627 sequence which had the following nucleotide sequence:

25 hybridization probe  
5'-ATGCTGGATGATGATGGGGACACCACCATGAGCCTGCATT-3' (SEQ ID NO:324).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1131 gene using the probe oligonucleotide and one of the PCR primers.

30 A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 144-146, and a stop signal at nucleotide positions 984-986 (Figure 229; SEQ ID NO:318). The predicted polypeptide precursor is 280 amino acids long, has a calculated molecular weight of approximately 31,966 daltons and an estimated pI of approximately 6.26. The transmembrane domain sequence is at about 49-74 of SEQ ID NO:319 and the region having sequence identity  
35 with LDL receptors is about 50-265 of SEQ ID NO:319. PRO1131 contains potential N-linked glycosylation sites at amino acid positions 95-98 and 169-172 of SEQ ID NO:319. Clone DNA59777-1480 has been deposited with the ATCC and is assigned ATCC deposit no. 203111.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 230 (SEQ ID NO:319), evidenced some sequence identity between the PRO1131 amino acid sequence and the following Dayhoff sequences: AB010710\_1, I49053, I49115, RNU56863\_1, LY4A\_MOUSE, I55686, MMU56404\_1, I49361, AF030313\_1 and MMU09739\_1.

EXAMPLE 102: Isolation of cDNA clones Encoding Human PRO1281

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein as DNA35720. Based on the DNA35720 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1281.

PCR primers (forward and reverse) were synthesized:

forward PCR primers:

5'-TGGAAGGCTGCCGCAACGACAATC-3' (SEQ ID NO:327);

5'-CTGATGTGGCCGATGTTCTG-3' (SEQ ID NO:328); and

5'-ATGGCTCAGTGTGCAGACAG-3' (SEQ ID NO:329).

reverse PCR primers:

5'-GCATGCTGCTCCGTGAAGTAGTCC-3' (SEQ ID NO:330); and

5'-ATGCATGGGAAAGAAGGCCTGCCC-3' (SEQ ID NO:331).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA35720 sequence which had the following nucleotide sequence:

hybridization probe:

5'-TGCACTGGTGACCACGAGGGGGTGCATATAGCCATCTGGAGCTGAG-3' (SEQ ID NO:332).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO1281 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated human fetal liver.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1281 (designated herein as DNA59820-1549 [Figure 232, SEQ ID NO:325]; and the derived protein sequence for PRO1281.

The entire coding sequence of PRO1281 is shown in Figure 232 (SEQ ID NO:325). Clone DNA59820-1549 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 228-230 and an apparent stop codon at nucleotide positions 2553-2555. The predicted polypeptide precursor is 775 amino acids long. The full-length PRO1281 protein shown in Figure 233 has an estimated molecular weight of about 85,481 daltons and a pI of about 6.92. Additional features include a signal peptide at about amino acids 1-15; and potential N-glycosylation sites at about amino acids 138-141 and 361-364.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 233 (SEQ ID NO:326), revealed some sequence

identity between the PRO1281 amino acid sequence and the following Dayhoff sequences: S44860, CET24D1\_1, CEC38H2\_3, CAC2\_HAECO, B3A2\_HUMAN, S22373, CEF38A3\_2, CEC34F6\_2, CEC34F6\_3, and CELT22B11\_3.

Clone DNA59820-1549 has been deposited with ATCC and is assigned ATCC deposit no. 203129.

5 EXAMPLE 103: Isolation of cDNA clones Encoding Human PRO1064

A cDNA sequence isolated in the amylase screen described in Example 2 above was found, by the WU-BLAST2 sequence alignment computer program, to have no significant sequence identity to any known human protein. This cDNA sequence is herein designated DNA45288. The DNA45288 sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence is herein designated DNA48609. Oligonucleotide primers based upon the DNA48609 sequence were then synthesized and employed to screen a human fetal kidney cDNA library which resulted in the identification of the DNA59827-1426 clone shown in Figure 234. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

20 The oligonucleotide probes employed were as follows:

forward PCR primer 5'-CTGAGACCCTGCAGCACCATCTG-3' (SEQ ID NO:336)

reverse PCR primer 5'-GGTGCTTCTTGAGCCCCACTTAGC-3' (SEQ ID NO:337)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA48609 sequence which had the following nucleotide sequence

25 hybridization probe

5'-AATCTAGCTTCTCCAGGACTGTGGTCGCCCCGTCCGCTGT-3' (SEQ ID NO:338)

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 532-534 and a stop signal at nucleotide positions 991-993 (Figure 234, SEQ ID NO:333). The predicted polypeptide precursor is 153 amino acids long, has a calculated molecular weight of approximately 17,317 daltons and an estimated pI of approximately 5.17. Analysis of the full-length PRO1064 sequence shown in Figure 235 (SEQ ID NO:334) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 24, a transmembrane domain from about amino acid 89 to about amino acid 110, an indole-3-glycerol phosphate synthase homology block from about amino acid 74 to about amino acid 105 and a Myb DNA binding domain protein repeat protein homology block from about amino acid 114 to about amino acid 137. Clone DNA59827-1426 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203089.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 235 (SEQ ID NO:334), evidenced homology between the PRO1064 amino acid sequence and the following Dayhoff sequences: MMNP15PRO\_1, BP187PLYH\_1, CELF42G8\_4, MMU58888\_1, GEN14270, TUB8\_SOLTU, RCN\_MOUSE, HUMRBSY79\_1, SESENODA\_1 and A21467\_1.

EXAMPLE 104: Isolation of cDNA clones Encoding Human PRO1379

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein DNA45232. Based on the DNA45232 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1379.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TGGACACCGTACCCTGGTATCTGC-3' (SEQ ID NO:341)

reverse PCR primer 5'-CCAACTCTGAGGAGAGCAAGTGGC-3' (SEQ ID NO:342)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA45232 sequence which had the following nucleotide sequence:

hybridization probe

5'-TGTATGTGCACACCCTCACCATCACCTCCAAGGGCAAGGAGAAC-3' (SEQ ID NO:343).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1379 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1379 which is designated herein as DNA59828-1608 and shown in Figure 237 (SEQ ID NO:339); and the derived protein sequence for PRO1379 (SEQ ID NO:340).

The entire coding sequence of PRO1379 is shown in Figure 237 (SEQ ID NO:339). Clone DNA59828-1608 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 10-12 and an apparent stop codon at nucleotide positions 1732-1734. The predicted polypeptide precursor is 574 amino acids long. The full-length PRO1379 protein shown in Figure 238 has an estimated molecular weight of about 65,355 daltons and a pI of about 8.73. Additional features include a signal peptide at about amino acids 1-17 and potential N-glycosylation sites at about amino acids 160-163, 287-290, and 323-326.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 238 (SEQ ID NO:340), revealed some homology between the PRO1379 amino acid sequence and the following Dayhoff sequences: YHY8\_YEAST, AF040625\_1, HP714394\_1, and HIV18U45630\_1.

Clone DNA59828-1608 has been deposited with ATCC and is assigned ATCC deposit no. 203158.

**EXAMPLE 105: Isolation of cDNA Clones Encoding Human PRO844**

An expressed sequence tag (EST) DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed sequence identity with aLP. Based on the information and discoveries provided herein, the clone for this EST, Incyte clone no. 2657496 from a cancerous lung library was further examined.

5 DNA sequencing of the insert for this clone gave a sequence (herein designated as DNA59838-1462; SEQ ID NO:344) which includes the full-length DNA sequence for PRO844 and the derived protein sequence for PRO844.

10 The entire nucleotide sequence of DNA59838-1462 is shown in Figure 239 (SEQ ID NO:344). Clone DNA59838-1462 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 5-7 and ending at the stop codon at nucleotide positions 338-340 of SEQ ID NO:344 (Figure 239). The predicted polypeptide precursor is 111 amino acids long (Figure 240). The full-length PRO844 protein shown in Figure 240 has an estimated molecular weight of about 12,050 daltons and a pI of about 5.45. Clone UNQ544 DNA59838-1462 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on  
15 known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO844 polypeptide suggests that it possesses significant sequence similarity to serine protease inhibitors, thereby indicating that PRO844 may be a novel proteinase inhibitor. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO844 amino acid sequence and at least the following Dayhoff  
20 sequences, ALK1\_HUMAN, P\_P82403, P\_P82402, ELAF\_HUMAN and P\_P60950.

**EXAMPLE 106: Isolation of cDNA Clones Encoding Human PRO848**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety  
25 of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a  
30 consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55999.

In light of an observed sequence homology between the DNA55999 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2768571, the Incyte EST clone 2768571 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.  
35 The sequence of this cDNA insert is shown in Figure 241 and is herein designated as DNA59839-1461.

The entire nucleotide sequence of DNA59839-1461 is shown in Figure 241 (SEQ ID NO:346). Clone DNA59839-1461 contains a single open reading frame with an apparent translational initiation site at nucleotide

positions 146-148 and ending at the stop codon at nucleotide positions 1946-1948 of SEQ ID NO:346 (Figure 241). The predicted polypeptide precursor is 600 amino acids long (Figure 242). The full-length PRO848 protein shown in Figure 242 has an estimated molecular weight of about 68,536 daltons. Clone DNA59839-1461 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO848 polypeptide suggests that it may be a novel sialyltransferase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO848 amino acid sequence and at least the following Dayhoff sequences, P\_R78619 (GalNAc-alpha-2, 6-sialyltransferase), CAAG5\_CHICK (alpha-n-acetylgalactosamide alpha-2, 6-sialyltransferase), HSU14550\_1, CAG6\_HUMAN and P\_R63217 (human alpha-2, 3-sialyltransferase).

#### EXAMPLE 107: Isolation of cDNA Clones Encoding Human PRO1097

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56006.

In light of an observed sequence homology between the DNA56006 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2408105, the Incyte EST clone 2408105 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 243 and is herein designated as DNA59841-1460.

The entire nucleotide sequence of DNA59841-1460 is shown in Figure 243 (SEQ ID NO:348). Clone DNA59841-1460 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 3-5 and ending at the stop codon at nucleotide positions 276-278 of SEQ ID NO:348 (Figure 243). The predicted polypeptide precursor is 91 amino acids long (Figure 244). The full-length PRO1097 protein shown in Figure 244 has an estimated molecular weight of about 10,542 daltons and a pI of about 10.04. Clone DNA59841-1460 has been deposited with ATCC on July 1, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analyzing Figure 244, the signal peptide is at about amino acids 1-20 of SEQ ID NO:349. The glycoprotease family protein domain starts at about amino acid 56, and the acyltransferase ChoActase/COT/CPT family peptide starts at about amino acid 49 of SEQ ID NO:349.

EXAMPLE 108: Isolation of cDNA clones Encoding Human PRO1153

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program “phrap” (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56008.

In light of an observed sequence homology between the DNA56008 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2472409, the Incyte EST clone 2472409 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 245 and is herein designated as DNA59842-1502.

The full length clone shown in Figure 245 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 92-94 and ending at the stop codon found at nucleotide positions 683-685 (Figure 245; SEQ ID NO:350). The predicted polypeptide precursor (Figure 246, SEQ ID NO:351) is 197 amino acids long. PRO1153 has a calculated molecular weight of approximately 21,540 daltons and an estimated pI of approximately 8.31. Clone DNA59842-1502 has been deposited with ATCC and is assigned ATCC deposit no. 209982. It is understood that the correct and actual sequence is in the deposited clone while herein are present representations based on current sequencing techniques which may have minor errors.

Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1153 shows some amino acid sequence identity to the following Dayhoff designations: S57447; SOYHRGPC\_1; S46965; P\_P82971; VCPHEROPH\_1; EXTN\_TOBAC; MLCB2548\_9; ANXA\_RABIT; JC5437 and SSGP\_VOLCA.

EXAMPLE 109: Isolation of cDNA clones Encoding Human PRO1154

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program “phrap” (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56025.



In light of an observed sequence homology between the DNA56025 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2169375, the Incyte EST clone 2169375 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 247 and is herein designated as DNA59846-1503.

The full length clone shown in Figure 247 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 86-88 and ending at the stop codon found at nucleotide positions 2909-2911 (Figure 247; SEQ ID NO:352). The predicted polypeptide precursor (Figure 248, SEQ ID NO:353) is 941 amino acids long. PRO1154 has a calculated molecular weight of approximately 107,144 daltons and an estimated pI of approximately 6.26. Clone DNA59846-1503 has been deposited with ATCC and is assigned ATCC deposit no. 209978.

Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1154 shows sequence identity to at least the following Dayhoff designations: AB011097\_1, AMPN\_HUMAN, RNU76997\_1, 159331, GEN14047, HSU62768\_1, P\_R51281, CET07F10\_1, SSU66371\_1, and AMPRE\_HUMAN.

EXAMPLE 110: Isolation of cDNA clones Encoding Human PRO1181

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database, designated herein as 82468. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56029.

In light of an observed sequence homology between the DNA56029 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2186536, the Incyte EST clone 2186536 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 249 and is herein designated as DNA59847-1511.

Clone DNA59847-1511 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 17-19 and ending at the stop codon at nucleotide positions 1328-1330 (Figure 249). The predicted polypeptide precursor is 437 amino acids long (Figure 250). The full-length PRO1181 protein shown in Figure 250 has an estimated molecular weight of about 46,363 daltons and a pI of about 6.22. Analysis of the full-length PRO1181 sequence shown in Figure 250 (SEQ ID NO:355) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15, potential N-glycosylation sites from about amino acid 46 to about amino acid 49, from about amino acid 189 to about amino acid 192 and from about amino acid 382 to about amino acid 385 and amino acid sequence blocks having homology to Ly-6/u-PAR domain proteins from about amino acid 287 to about amino acid 300 and from about amino acid

98 to about amino acid 111. Clone DNA59847-1511 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203098.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 250 (SEQ ID NO:355), evidenced homology between the PRO1181 amino acid sequence and the following Dayhoff sequences: AF041083\_1, P\_W26579, RNMAGPIAN\_1, CELT13C2\_2, LMSAP2GN\_1, S61882, CEF35C5\_12, DP87\_DICDI, GIU47631\_1 and P\_R07092.

**EXAMPLE 111: Isolation of cDNA clones Encoding Human PRO1182**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database, designated herein as 146647. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56033.

In light of an observed sequence homology between the DNA56033 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2595195, the Incyte EST clone 2595195 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 251 and is herein designated as DNA59848-1512.

Clone DNA59848-1512 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 67-69 and ending at the stop codon at nucleotide positions 880-882 (Figure 251). The predicted polypeptide precursor is 271 amino acids long (Figure 252). The full-length PRO1182 protein shown in Figure 252 has an estimated molecular weight of about 28,665 daltons and a pI of about 5.33. Analysis of the full-length PRO1182 sequence shown in Figure 252 (SEQ ID NO:357) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25, an amino acid block having homology to C-type lectin domain proteins from about amino acid 247 to about amino acid 256 and an amino acid sequence block having homology to C1q domain proteins from about amino acid 44 to about amino acid 77. Clone DNA59848-1512 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203088.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 252 (SEQ ID NO:357), evidenced significant homology between the PRO1182 amino acid sequence and the following Dayhoff sequences: PSPD\_BOVIN, CL43\_BOVIN, CONG\_BOVIN, P\_W18780, P\_R45005, P\_R53257 and CELEGAP7\_1.

**EXAMPLE 112: Isolation of cDNA clones Encoding Human PRO1155**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program “phrap” (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56102.

In light of an observed sequence homology between the DNA56102 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2858870, the Incyte EST clone 2858870 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 253 and is herein designated as DNA59849-1504.

The full length clone shown in Figure 253 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 158-160 and ending at the stop codon found at nucleotide positions 563-565 (Figure 253; SEQ ID NO:358). The predicted polypeptide precursor (Figure 254, SEQ ID NO:359) is 135 amino acids long. PRO1155 has a calculated molecular weight of approximately 14,833 daltons and an estimated pI of approximately 9.78. Clone DNA59849-1504 has been deposited with ATCC and is assigned ATCC deposit no. 209986. It is understood that the actual clone has the correct sequence whereas herein are only representations which are prone to minor sequencing errors.

Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1155 shows some amino acid sequence identity with the following Dayhoff designations: TKNK\_BOVIN; PVB19X587\_1; AF019049\_1; P\_W00948; S72864; P\_W00949; I62742; AF038501\_1; TKNG\_HUMAN; and YAT1\_RHOBL. Based on the information provided herein, PRO1155 may play a role in providing neuroprotection and cognitive enhancement.

**EXAMPLE 113: Isolation of cDNA clones Encoding Human PRO1156**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database, designated herein as 138851. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program “phrap” (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56261.

In light of an observed sequence homology between the DNA56261 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3675191, the Incyte EST clone 3675191 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 255 and is herein designated as DNA59853-1505.

The full length clone shown in Figure 255 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 212-214 and ending at the stop codon found at nucleotide positions 689-691 (Figure 255; SEQ ID NO:360). The predicted polypeptide precursor (Figure 256, SEQ ID NO:361) is 159 amino acids long. PRO1156 has a calculated molecular weight of approximately 17,476 daltons, an estimated pI of approximately 9.15, a signal peptide sequence at about amino acids 1 to about 22, and potential N-glycosylation sites at about amino acids 27-30 and 41-44.

Clone DNA59853-1505 was deposited with the ATCC on June 16, 1998 and is assigned ATCC deposit no. 209985.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence shown in Figure 256 (SEQ ID NO:361), revealed some homology between the PRO1156 amino acid sequence and the following Dayhoff sequences: D45027\_1, P\_R79914, JC5309, KBF2\_HUMAN, AF010144\_1, GEN14351, S68681, P\_R79915, ZMTAC\_3, and HUMCPGO\_1.

#### EXAMPLE 114: Isolation of cDNA Clones Encoding Human PRO1098

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56377.

In light of an observed sequence homology between the DNA56377 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3050917, the Incyte EST clone 3050917 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 257 and is herein designated as DNA59854-1459.

The entire nucleotide sequence of DNA59854-1459 is shown in Figure 257 (SEQ ID NO:362). Clone DNA59854-1459 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 58-60 and ending at the stop codon at nucleotide positions 292-294 of SEQ ID NO:362 (Figure 257). The predicted polypeptide precursor is 78 amino acids long (Figure 258). The full-length PRO1098 protein shown in Figure 258 has an estimated molecular weight of about 8,396 daltons and a pI of about 7.66. Clone DNA59854-1459 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone

has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analyzing Figure 258, a signal peptide appears to be at about amino acids 1-19 of SEQ ID NO:363, an N-glycosylation site appears to be at about amino acids 37-40 of SEQ ID NO:363, and N-myristoylation sites appear to be at about 15-20, 19-24 and 60-65 of SEQ ID NO:363.

#### EXAMPLE 115: Isolation of cDNA clones Encoding Human PRO1127

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57959.

In light of an observed sequence homology between the DNA57959 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 685126, the Merck EST clone 685126 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 259 and is herein designated as DNA60283-1484.

The full length clone shown in Figure 259 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 126-128 and ending at the stop codon found at nucleotide positions 327-329 (Figure 259; SEQ ID NO:364). The predicted polypeptide precursor (Figure 260, SEQ ID NO:365) is 67 amino acids long including a signal peptide at about 1-29 of SEQ ID NO:365. PRO1127 has a calculated molecular weight of approximately 7,528 daltons and an estimated pI of approximately 4.95. Clone DNA60283-1484 was deposited with the ATCC on July 1, 1998 and is assigned ATCC deposit no. 203043. It is understood that the deposited clone has the actual sequence, whereas representations which may have minor sequencing errors are presented herein.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 260 (SEQ ID NO:365), revealed some homology between the PRO1127 amino acid sequence and the following Dayhoff sequences: AF037218\_48, P\_W09638, HBA\_HETPO, S39821, KR2\_EBV, CET20D3\_8, HCU37630\_1, HS193B12\_10, S40012 and TRITUBC\_1.

#### EXAMPLE 116: Isolation of cDNA clones Encoding Human PRO1126

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a

proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program “phrap” (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56250.

In light of an observed sequence homology between the DNA56250 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1437250, the Incyte EST clone 1437250 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 261 and is herein designated as DNA60615-1483.

Clone DNA60615-1483 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 110-112 and ending at the stop codon at nucleotide positions 1316-1318 (Figure 261). The predicted polypeptide precursor is 402 amino acids long (Figure 262). The full-length PRO1126 protein shown in Figure 262 has an estimated molecular weight of about 45,921 daltons and a pI of about 8.60. Analysis of the full-length PRO1126 sequence shown in Figure 262 (SEQ ID NO:367) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25 and potential N-glycosylation sites from about amino acid 66 to about amino acid 69, from about amino acid 138 to about amino acid 141 and from about amino acid 183 to about amino acid 186. Clone DNA60615-1483 has been deposited with ATCC on June 16, 1998 and is assigned ATCC deposit no. 209980.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 262 (SEQ ID NO:367), evidenced significant homology between the PRO1126 amino acid sequence and the following Dayhoff sequences: I73636, NOMR\_HUMAN, MMUSMYOC3\_1, HS454G6\_1, P\_R98225, RNU78105\_1, RNU72487\_1, AF035301\_1, CEELC48E7\_4 and CEF11C3\_3.

#### EXAMPLE 117: Isolation of cDNA clones Encoding Human PRO1125

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program “phrap” (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56540.

In light of an observed sequence homology between the DNA56540 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1486114, the Incyte EST clone 1486114 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.

The sequence of this cDNA insert is shown in Figure 263 and is herein designated as DNA60615-1483.

The full length clone shown in Figure 263 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 47-49 and ending at the stop codon found at nucleotide positions 1388-1390 (Figure 263; SEQ ID NO:368). The predicted polypeptide precursor (Figure 264, SEQ ID NO:369) is 447 amino acids long. PRO1125 has a calculated molecular weight of approximately 49,798 daltons and an estimated pI of approximately 9.78. Clone DNA60619-1482 has been deposited with ATCC and is assigned ATCC deposit no. 209993. It is understood that the clone has the actual sequence and that the sequences herein are representations based on current techniques which may be prone to minor errors.

Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1125 shows some sequence identity with the following Dayhoff designations: RCO1\_NEUCR; S58306; PKWA\_THECU; S76086; P\_R85881; HET1\_PODAN; SPU92792\_1; APAF\_HUMAN; S76414 and S59317.

#### EXAMPLE 118: Isolation of cDNA clones Encoding Human PRO1186

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56748.

In light of an observed sequence homology between the DNA56748 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3476792, the Incyte EST clone 3476792 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 265 and is herein designated as DNA60621-1516.

The full length clone shown in Figure 265 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 91-93 and ending at the stop codon found at nucleotide positions 406-408 (Figure 265; SEQ ID NO:370). The predicted polypeptide precursor (Figure 266, SEQ ID NO:371) is 105 amino acids long. The signal peptide is at amino acids 1-19 of SEQ ID NO:371. PRO1186 has a calculated molecular weight of approximately 11,715 daltons and an estimated pI of approximately 9.05. Clone DNA60621-1516 was deposited with the ATCC on August 4, 1998 and is assigned ATCC deposit no. 203091.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 266 (SEQ ID NO:371), revealed some sequence identity between the PRO1186 amino acid sequence and the following Dayhoff sequences: VPRA\_DENPO, LFE4\_CHICK, AF034208\_1, AF030433\_1, A55035, COL\_RABIT, CELB0507\_9, S67826\_1, S34665 and

CRU73817\_1.

**EXAMPLE 119: Isolation of cDNA clones Encoding Human PRO1198**

An initial DNA sequence referred to herein as DNA52083 was identified using a yeast screen in a human umbilical vein endothelial cell cDNA library that preferentially represents the 5' ends of the primary cDNA clones. DNA52083 was compared to ESTs from public databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA), using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. The ESTs were clustered and assembled into a consensus DNA sequence using the computer program "phrap" (Phil Green, University of Washington, Seattle, Washington). One or more of the ESTs was obtained from human breast skin tissue biopsy. This consensus sequence is designated herein as DNA52780.

In light of an observed sequence homology between the DNA52780 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3852910, the Incyte EST clone 3852910 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 267 and is herein designated as DNA60622-1525.

The full length DNA60622-1525 clone shown in Figure 267 (SEQ ID NO:372) contained a single open reading frame with an apparent translational initiation site at nucleotide positions 54 to 56 and ending at the stop codon found at nucleotide positions 741 to 743. The predicted polypeptide precursor, which is shown in Figure 268 (SEQ ID NO:373), is 229 amino acids long. PRO1198 has a calculated molecular weight of approximately 25,764 daltons and an estimated pI of approximately 9.17. There is a signal peptide sequence at about amino acids 1 through 34. There is sequence identity with glycosyl hydrolases family 31 protein at about amino acids 142 to about 175.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 268 (SEQ ID NO:373), revealed some homology between the PRO1198 amino acid sequence and the following Dayhoff sequences: ATF6H11\_6, UCRI\_RAT, TOBSUP2NT\_1, RCUERF3\_1, AMU88186\_1, P\_W22485, S56579, AF040711\_1, DPP4\_PIG.

Clone DNA60622-1525 was been deposited with the ATCC on August 4, 1998, and is assigned ATCC deposit no. 203090.

**EXAMPLE 120: Isolation of cDNA clones Encoding Human PRO1158**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle,



Washington). The consensus sequence obtained therefrom is herein designated DNA57248.

In light of an observed sequence homology between the DNA57248 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2640776, the Incyte EST clone 2640776 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 269 and is herein designated as DNA60625-1507.

The full length clone shown in Figure 269 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 163 to 165 and ending at the stop codon found at nucleotide positions 532 to 534 (Figure 269; SEQ ID NO:374). The predicted polypeptide precursor (Figure 270, SEQ ID NO:375) is 123 amino acids long. PRO1158 has a calculated molecular weight of approximately 13,113 daltons and an estimated pI of approximately 8.53. Additional features include a signal peptide sequence at about amino acids 1-19, a transmembrane domain at about amino acids 56-80, and a potential N-glycosylation site at about amino acids 36-39. Clone DNA60625-1507 was deposited with the ATCC on June 16, 1998 and is assigned ATCC deposit no. 209975.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 270 (SEQ ID NO:375), revealed some homology between the PRO1158 amino acid sequence and the following Dayhoff sequences: ATAC00310510F18A8.10, P\_R85151, PHS2\_SOLTU, RNMHCIBAC\_1, RNA1FMHC\_1, I68771, RNRT1A10G\_1, PTPA\_HUMAN, HUMGACA\_1, and CHKPTPA\_1.

#### EXAMPLE 121: Isolation of cDNA clones Encoding Human PRO1159

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57221.

In light of an observed sequence homology between the DNA57221 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 376776, the Incyte EST clone 376776 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 271 and is herein designated as DNA60627-1508.

Clone DNA60627-1508 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 92-94 and ending at the stop codon at nucleotide positions 362-364 (Figure 271). The predicted polypeptide precursor is 90 amino acids long (Figure 272). The full-length PRO1159 protein shown in Figure 272 has an estimated molecular weight of about 9,840 daltons and a pI of about 10.13. Analysis of the full-length PRO1159 sequence shown in Figure 272 (SEQ ID NO:377) evidences the presence

of the following: a signal peptide from about amino acid 1 to about amino acid 15 and a potential N-glycosylation site from about amino acid 38 to about amino acid 41. Clone DNA60627-1508 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203092.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 272 (SEQ ID NO:377), evidenced significant homology between the PRO1159 amino acid sequence and the following Dayhoff sequences: AF016494\_6, AF036708\_20, DSSCUTE\_1, D89100\_1, S28060, MEFA\_XENLA, AF020798\_12, G70065, E64423, JQ2005.

EXAMPLE 122: Isolation of cDNA clones Encoding Human PRO1124

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56035.

In light of an observed sequence homology between the DNA56035 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2767646, the Incyte EST clone 2767646 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 273 and is herein designated as DNA60629-1481.

The full length clone shown in Figure 273 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 25-27 and ending at the stop codon found at nucleotide positions 2782-2784 (Figure 273; SEQ ID NO:378). The predicted polypeptide precursor (Figure 274, SEQ ID NO:379) is 919 amino acids long. PRO1124 has a calculated molecular weight of approximately 101,282 daltons and an estimated pI of approximately 5.37. Clone DNA60629-1481 has been deposited with the ATCC and is assigned ATCC deposit no. 209979. It is understood that the deposited clone has the actual sequence, whereas only representations based on current sequencing techniques which may include normal and minor errors, are provided herein.

Based on a WU-BLAST2 sequence alignment analysis of the full-length sequence, PRO1124 shows significant amino acid sequence identity to a chloride channel protein and to ECAM-1. Specifically, the following Dayhoff designations were identified as having sequence identity with PRO1124: ECLC\_BOVIN, AF001261\_1, P\_W06548, SSC6A10\_1, AF004355\_1, S76691, AF017642, BYU06866\_2, CSA\_DICDI and SAU47139\_2.

EXAMPLE 123: Isolation of cDNA clones Encoding Human PRO1287

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed homology to the fringe protein. This EST sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence obtained is herein designated DNA40568.

Based on the DNA40568 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1287. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, *supra*, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTCGGGGAAAGGGACTTGATGTTGG-3' (SEQ ID NO:382)

reverse PCR primer 1 5'-GCGAAGGTGAGCCTCTATCTCGTGCC-3' (SEQ ID NO:383)

reverse PCR primer 2 5'-CAGCCTACACGTATTGAGG-3' (SEQ ID NO:384)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40568 sequence which had the following nucleotide sequence

hybridization probe

5'-CAGTCAGTACAATCCTGGCATAATATACGGCCACCATGATGCAGTCCC-3' (SEQ ID NO:385).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO1287 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human bone marrow tissue. The cDNA libraries used to isolated the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1287 (designated herein as DNA61755-1554 [Figure 275, SEQ ID NO:380]) and the derived protein sequence for PRO1287.

The entire nucleotide sequence of DNA61755-1554 is shown in Figure 275 (SEQ ID NO:380). The full length clone contained a single open reading frame with an apparent translational initiation site at nucleotide positions 655-657 and a stop signal at nucleotide positions 2251-2253 (Figure 275, SEQ ID NO:380). The predicted polypeptide precursor is 532 amino acids long, has a calculated molecular weight of approximately 61,351 daltons and an estimated pI of approximately 8.77. Analysis of the full-length PRO1287 sequence shown in Figure 276 (SEQ ID NO:381) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 27 and potential N-glycosylation sites from about amino acid 315 to about amino acid 318 and from about amino acid 324 to about amino acid 327. Clone DNA61755-1554 has been deposited with ATCC on August 11, 1998 and is assigned ATCC deposit no. 203112.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 276 (SEQ ID NO:381), evidenced significant homology between the PRO1287 amino acid sequence and the following Dayhoff sequences: CET24D1\_1, EZRI\_BOVIN, GGU19889\_1, CC3\_YEAST, S74244, NALS\_MOUSE, MOES\_PIG, S28660, S44860 and YNA4\_CAEL.

#### EXAMPLE 124: Isolation of cDNA clones Encoding Human PRO1312

DNA55773 was identified in a human fetal kidney cDNA library using a yeast screen that preferentially represents the 5' ends of the primary cDNA clones. Based on the DNA55773 sequence, oligonucleotides were synthesized for use as probes to isolate a clone of the full-length coding sequence for PRO1312.

The full length DNA61873-1574 clone shown in Figure 277 (SEQ ID NO:386) contained a single open reading frame with an apparent translational initiation site at nucleotide positions 7-9 and ending at the stop codon found at nucleotide positions 643-645. The predicted polypeptide precursor is 212 amino acids long (Figure 278, SEQ ID NO:387). PRO1312 has a calculated molecular weight of approximately 24,024 daltons and an estimated pI of approximately 6.26. Other features include a signal peptide at about amino acids 1-14; a transmembrane domain at about amino acids 141-160, and potential N-glycosylation sites at about amino acids 76-79 and 93-96.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 278 (SEQ ID NO:387), revealed some homology between the PRO1312 amino acid sequence and the following Dayhoff sequences: GCINTALPH\_1, GIBMUC1A\_1, P\_R96298, AF001406\_1, PVU88874\_1, P\_R85151, AF041409\_1, CELC50F2\_7, C45875, and AB009510\_21.

Clone DNA61873-1574 has been deposited with ATCC and is assigned ATCC deposit no. 203132.

**EXAMPLE 125: Isolation of cDNA clones Encoding Human PRO1192**

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein DNA35924. Based on the DNA35924 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1192.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'-CCGAGGCCATCTAGAGGCCAGAGC-3' (SEQ ID NO:390)

reverse PCR primer: 5'-ACAGGCAGAGCCAATGGCCAGAGC-3' (SEQ ID NO:391).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35924 sequence which had the following nucleotide sequence:

hybridization probe:

5'-GAGAGGACTGCGGGAGTTTGGGACCTTTGTGCAGACGTGCTCATG-3' (SEQ ID NO:392).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1192 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver and spleen tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1192 designated herein as DNA62814-1521 and shown in Figure 279 (SEQ ID NO:388); and the derived protein sequence for PRO1192 which is shown in Figure 280 (SEQ ID NO:389).

The entire coding sequence of PRO1192 is shown in Figure 279 (SEQ ID NO:388). Clone DNA62814-1521 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and an apparent stop codon at nucleotide positions 766-768. The predicted polypeptide precursor is 215 amino acids long. The predicted polypeptide precursor has the following features: a signal peptide at about amino acids 1-21; a transmembrane domain at about amino acids 153-176; potential N-glycosylation sites at about amino acids 39-42 and 118-121; and homology with myelin P0 proteins at about amino acids 27-68 and 99-128 of Figure 280. The full-length PRO1192 protein shown in Figure 280 has an estimated molecular weight of about 24,484 daltons and a pI of about 6.98.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 280 (SEQ ID NO:389), revealed homology between the PRO1192 amino acid sequence and the following Dayhoff sequences: GEN12838, MYP0\_HUMAN, AF049498\_1, GEN14531, P\_W14146, HS46KDA\_1, CINB\_RAT, OX2G\_RAT, D87018\_1, and D86996\_2.

Clone DNA62814-1521 was deposited with the ATCC on August 4, 1998, and is assigned ATCC deposit no. 203093.

**EXAMPLE 126: Isolation of cDNA clones Encoding Human PRO1160**

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described

in Example 1 above This consensus sequence is herein designated DNA40650. Based on the DNA40650 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1160.

PCR primers (forward and reverse) were synthesized:

5 forward PCR primer 5'-GCTCCCTGATCTTCATGTCACCACC-3' (SEQ ID NO:395) .

reverse PCR primer 5'-CAGGGACACACTCTACCATTCTGGGAG-3' (SEQ ID NO:396)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40650 sequence which had the following nucleotide sequence

hybridization probe

10 5'-CCATCTTTCTGGTCTCTGCCCAGAATCCGACAACAGCTGCTC-3' (SEQ ID NO:397)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1160 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast tissue.

15 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1160 (designated herein as DNA62872-1509 [Figure 281, SEQ ID NO: 393]) and the derived protein sequence for PRO1160.

The entire nucleotide sequence of DNA62872-1509 is shown in Figure 281 (SEQ ID NO:393). Clone DNA62872-1509 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 40-42 and ending at the stop codon at nucleotide positions 310-312 (Figure 281). The predicted polypeptide precursor is 90 amino acids long (Figure 282). The full-length PRO1160 protein shown in Figure 282 has an estimated molecular weight of about 9,039 daltons and a pI of about 4.37. Analysis of the full-length PRO1160 sequence shown in Figure 282 (SEQ ID NO:394) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19 and a protein kinase C phosphorylation site from about amino acid 68 to about amino acid 70. Clone DNA62872-1509 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203100.

25 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 282 (SEQ ID NO:394), evidenced significant homology between the PRO1160 amino acid sequence and the following Dayhoff sequences: B30305, GEN13490, I53641, S53363, HA34\_BRELC, SP96\_DICDI, S36326, SSU51197\_10, MUC1\_XENLA, TCU32448\_1 and AF000409\_1.

#### EXAMPLE 127: Isolation of cDNA clones Encoding Human PRO1187

35 Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing

homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57726.

5 In light of an observed sequence homology between the DNA57726 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 358563, the Incyte EST clone 358563 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 283 and is herein designated as DNA62876-1517.

10 The full length clone shown in Figure 283 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and ending at the stop codon found at nucleotide positions 481-483 (Figure 283; SEQ ID NO:398). The predicted polypeptide precursor (Figure 284, SEQ ID NO:399) is 120 amino acids long. The signal peptide is at about amino acids 1-17 of SEQ ID NO:399. PRO1187 has a calculated molecular weight of approximately 12,925 daltons and an estimated pI of approximately 9.46. Clone DNA62876-1517 was deposited with the ATCC on August 4, 1998 and is assigned  
15 ATCC deposit no. 203095. It is understood that the deposited clone contains the actual sequence and that the representations herein may have minor sequencing errors.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 284 (SEQ ID NO:399), revealed some sequence identity (and therefore some relation) between the PRO1187 amino acid sequence and the following Dayhoff  
20 sequences: MGNENDOBX\_1, CELF41G3\_9, AMPG\_STRLI, HSBBOVHERL\_2, LEEXTEN10\_1, AF029958\_1 and P\_W04957.

#### EXAMPLE 128: Isolation of cDNA clones Encoding Human PRO1185

25 Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70  
30 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56426.

In light of an observed sequence homology between the DNA56426 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3284411, the Incyte EST clone 3284411 was purchased  
35 and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 285 and is herein designated as DNA62881-1515.

The full length DNA62881-1515 clone shown in Figure 285 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 4-6 and ending at the stop codon found at nucleotide positions 598-600 (Figure 285; SEQ ID NO:400). The predicted polypeptide precursor (Figure 286, SEQ ID NO:401) is 198 amino acids long. The signal peptide is at about amino acids 1-21 of SEQ ID NO:401. PRO1185 has a calculated molecular weight of approximately 22,105 daltons and an estimated pI of approximately 7.73. Clone DNA62881-1515 has been deposited with the ATCC and is assigned ATCC deposit no. 203096.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 286 (SEQ ID NO:401), revealed some sequence identity between the PRO1185 amino acid sequence and the following Dayhoff sequences: TUP1\_YEAST, AF041382\_1, MAOM\_SOLTU, SPPBPHU9\_1,I41024, EPCPLCFAIL\_1, HSPLEC\_1, YKL4\_CAEEL, A44643, TGU65922\_1.

#### EXAMPLE 129: Isolation of cDNA clones Encoding Human PRO1345

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA47364. Based on the DNA47364 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1345.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CCTGGTTATCCCCAGGAAGTCCGAC-3' (SEQ ID NO:404)

reverse PCR primer 5'-CTCTTGCTGCTGCGACAGGCCTC-3' (SEQ ID NO:405)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47364 sequence which had the following nucleotide sequence

hybridization probe

5'-CGCCCTCCAAGACTATGGTAAAAGGAGCCTGCCAGGTGTCAATGAC-3' (SEQ ID NO:406)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1345 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast carcinoma tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1345 (designated herein as DNA64852-1589 [Figure 287, SEQ ID NO:402]) and the derived protein sequence for PRO1345.

The entire nucleotide sequence of DNA64852-1589 is shown in Figure 287 (SEQ ID NO:402). Clone DNA64852-1589 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 7-9 or 34-36 and ending at the stop codon at nucleotide positions 625-627 (Figure 287). The predicted polypeptide precursor is 206 amino acids long (Figure 288). The full-length PRO1345 protein shown in Figure 288 has an estimated molecular weight of about 23,190 daltons and a pI of about 9.40. Analysis of



the full-length PRO1345 sequence shown in Figure 288 (SEQ ID NO:403) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 31 or from about amino acid 10 to about amino acid 31 and a C-type lectin domain signature sequence from about amino acid 176 to about amino acid 190. Clone DNA64852-1589 has been deposited with ATCC on August 18, 1998 and is assigned ATCC deposit no. 203127.

5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 288 (SEQ ID NO:403), evidenced significant homology between the PRO1345 amino acid sequence and the following Dayhoff sequences: BTU22298\_1, TETN\_CARSP, TETN\_HUMAN, MABA\_RAT, S34198, P\_W13144, MACMBPA\_1, A46274, PSPD\_RAT AND P\_R32188.

10 EXAMPLE 130: Isolation of cDNA clones Encoding Human PRO1245

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a  
15 proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle,  
20 Washington). The consensus sequence obtained therefrom is herein designated DNA56019.

In light of an observed sequence homology between the DNA56019 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1327836, the Incyte EST clone 1327836 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 289 and is herein designated as DNA64884-1527.

25 The full length clone shown in Figure 289 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 79-81 and ending at the stop codon found at nucleotide positions 391-393 (Figure 289; SEQ ID NO:407). The predicted polypeptide precursor (Figure 290, SEQ ID NO:408) is 104 amino acids long, with a signal peptide sequence at about amino acid 1 to about amino acid 18. PRO1245 has a calculated molecular weight of approximately 10,100 daltons and an estimated pI of  
30 approximately 8.76.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 290 (SEQ ID NO:408), revealed some homology between the PRO1245 amino acid sequence and the following Dayhoff sequences: SYA\_THETH, GEN11167, MTV044\_4, AB011151\_1, RLAJ2750\_3, SNELIPTRA\_1, S63624, C28391, A37907, and  
35 S14064.

Clone DNA64884-1245 was deposited with the ATCC on August 25, 1998 and is assigned ATCC deposit no. 203155.

**EXAMPLE 131: Isolation of cDNA clones Encoding Human PRO1358**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program “phrap” (Phil Green, University of Washington, Seattle, Washington).

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 88718, the Incyte EST clone 88718 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 291 and is herein designated as DNA64890-1612.

The full length clone shown in Figure 291 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 86 through 88 and ending at the stop codon found at nucleotide positions 1418 through 1420 (Figure 291; SEQ ID NO:409). The predicted polypeptide precursor (Figure 292, SEQ ID NO:410) is 444 amino acids long. The signal peptide is at about amino acids 1-18 of SEQ ID NO:410. PRO1358 has a calculated molecular weight of approximately 50,719 daltons and an estimated pI of approximately 8.82. Clone DNA64890-1612 was deposited with the ATCC on August 18, 1998 and is assigned ATCC deposit no. 203131.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 292 (SEQ ID NO:410), revealed sequence identity between the PRO1358 amino acid sequence and the following Dayhoff sequences: P\_W07607, AB000545\_1, AB000546\_1, A1AT\_RAT, AB015164\_1, P\_P50021, COTR\_CAVPO, and HAMHPP\_1. The variants claimed in this application exclude these sequences.

**EXAMPLE 132: Isolation of cDNA clones Encoding Human PRO1195**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program “phrap” (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55716.

In light of an observed sequence homology between the DNA55716 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3252980, the Incyte EST clone 3252980 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 293 and is herein designated as DNA65412-1523.

The full length clone shown in Figure 293 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 58-60 and ending at the stop codon found at nucleotide positions 511-513 (Figure 293; SEQ ID NO:411). The predicted polypeptide precursor (Figure 294, SEQ ID NO:412) is 151 amino acids long. The signal sequence is at about amino acids 1-22 of SEQ ID NO:412. PRO1195 has a calculated molecular weight of approximately 17,277 daltons and an estimated pI of approximately 5.33. Clone DNA65412-1523 was deposited with the ATCC on August 4, 1998 and is assigned ATCC deposit no. 203094.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 294 (SEQ ID NO:412), revealed some sequence identity between the PRO1195 amino acid sequence and the following Dayhoff sequences: MMU28486\_1, AF044205\_1, P\_W31186, CELK03C7\_1, F69034, EF1A\_METVA, AF024540\_1, SSU90353\_1, MRSP\_STAAU and P\_R97680.

#### EXAMPLE 133: Isolation of cDNA clones Encoding Human PRO1270

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57951.

In light of an observed sequence homology between the DNA57951 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 124878, the Merck EST clone 124878 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 295 and is herein designated as DNA66308-1537.

Clone DNA66308-1537 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 103-105 and ending at the stop codon at nucleotide positions 1042-1044 (Figure 295). The predicted polypeptide precursor is 313 amino acids long (Figure 296). The full-length PRO1270 protein shown in Figure 296 has an estimated molecular weight of about 34,978 daltons and a pI of about 5.71. Analysis of the full-length PRO1270 sequence shown in Figure 296 (SEQ ID NO:414) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 16, a potential N-glycosylation site from about amino acid 163 to about amino acid 166 and glycosaminoglycan attachment sites from about

amino acid 74 to about amino acid 77 and from about amino acid 289 to about amino acid 292. Clone DNA66308-1537 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203159.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 296 (SEQ ID NO:414), evidenced significant homology between the PRO1270 amino acid sequence and the following Dayhoff sequences: XLU86699\_1, S49589, FIBA\_PARPA, FIBB\_HUMAN, P\_R47189, AF004326\_1, DRTENASCN\_1, AF004327\_1, P\_W01411 and FIBG\_BOVIN.

**EXAMPLE 134: Isolation of cDNA clones Encoding Human PRO1271**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57955.

In light of an observed sequence homology between the DNA57955 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA625350, the Merck EST clone AA625350 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 297 and is herein designated as DNA66309-1538.

Clone DNA66309-1538 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 94-96 and ending at the stop codon at nucleotide positions 718-720 (Figure 297). The predicted polypeptide precursor is 208 amino acids long (Figure 298). The full-length PRO1271 protein shown in Figure 298 has an estimated molecular weight of about 21,531 daltons and a pI of about 8.99. Analysis of the full-length PRO1271 sequence shown in Figure 298 (SEQ ID NO:416) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 31 and a transmembrane domain from about amino acid 166 to about amino acid 187. Clone DNA66309-1538 has been deposited with ATCC on September 15, 1998 and is assigned ATCC deposit no. 203235.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 298 (SEQ ID NO:416), evidenced significant homology between the PRO1271 amino acid sequence and the following Dayhoff sequences: S57180, S63257, AGA1\_YEAST, BPU43599\_1, YS8A\_CAEEL, S67570, LSU54556\_2, S70305, VGLX\_HSVEB, and D88733\_1.

**EXAMPLE 135: Isolation of cDNA clones Encoding Human PRO1375**

A Merck/Wash. U. database was searched and a Merck EST was identified. This sequence was then put in a program which aligns it with other sequences from the Swiss-Prot public database, public EST databases (e.g., GenBank, Merck/Wash. U.), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)] as a comparison of the extracellular domain (ECD) protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program “phrap” (Phil Green, University of Washington, Seattle, Washington).

A consensus DNA sequence was assembled relative to other EST sequences using phrap. This consensus sequence is designated herein “DNA67003”.

Based on the DNA67003 consensus sequence, the nucleic acid (SEQ ID NO:417) was identified in a human pancreas library. DNA sequencing of the clone gave the full-length DNA sequence for PRO1375 and the derived protein sequence for PRO1375.

The entire coding sequence of PRO1375 is shown in Figure 299 (SEQ ID NO:417). Clone DNA67004-1614 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 104-106 and an apparent stop codon at nucleotide positions 698-700 of SEQ ID NO:417. The predicted polypeptide precursor is 198 amino acids long. The transmembrane domains are at about amino acids 11-28 (type II) and 103-125 of SEQ ID NO:418. Clone DNA67004-1614 has been deposited with ATCC and is assigned ATCC deposit no. 203115. The full-length PRO1375 protein shown in Figure 300 has an estimated molecular weight of about 22,531 daltons and a pI of about 8.47.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 300 (SEQ ID NO:418), revealed sequence identity between the PRO1375 amino acid sequence and the following Dayhoff sequences: AF026198\_5, CELR12C12\_5, S73465, Y011\_MYCPN, S64538\_1, P\_P8150, MUVSHPO10\_1, VSH\_MUMPL and CVU59751\_5.

**EXAMPLE 136: Isolation of cDNA clones Encoding Human PRO1385**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program “phrap” (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57952.

In light of an observed sequence homology between the DNA57952 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3129630, the Incyte EST clone 3129630 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 301 and is herein designated as DNA68869-1610.

Clone DNA68869-1610 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 26-28 and ending at the stop codon at nucleotide positions 410-412 (Figure 301). The predicted polypeptide precursor is 128 amino acids long (Figure 302). The full-length PRO1385 protein shown in Figure 302 has an estimated molecular weight of about 13,663 daltons and a pI of about 10.97. Analysis of the full-length PRO1385 sequence shown in Figure 302 (SEQ ID NO:420) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, and glycosylaminoglycan attachment sites from about amino acid 82 to about amino acid 85 and from about amino acid 91 to about amino acid 94. Clone DNA68869-1610 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203164.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 302 (SEQ ID NO:420), evidenced low homology between the PRO1385 amino acid sequence and the following Dayhoff sequences: CELT14A8\_1, LMNACHRA1\_1, HXD9\_HUMAN, CHKCMLF\_1, HS5PP34\_2, DMDRING\_1, A37107\_1, MMLUNGENE\_1, PUM\_DROME and DMU25117\_1.

#### EXAMPLE 137: Isolation of cDNA clones Encoding Human PRO1387

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56259.

In light of an observed sequence homology between the DNA56259 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3507924, the Incyte EST clone 3507924 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 303 and is herein designated as DNA68872-1620.

Clone DNA68872-1620 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 85-87 and ending at the stop codon at nucleotide positions 1267-1269 (Figure 303). The predicted polypeptide precursor is 394 amino acids long (Figure 304). The full-length PRO1387 protein shown in Figure 304 has an estimated molecular weight of about 44,339 daltons and a pI of about 7.10. Analysis of the full-length PRO1387 sequence shown in Figure 304 (SEQ ID NO:422) evidences the presence

of the following: a signal peptide from about amino acid 1 to about amino acid 19, a transmembrane domain from about amino acid 275 to about amino acid 296, potential N-glycosylation sites from about amino acid 76 to about amino acid 79, from about amino acid 231 to about amino acid 234, from about amino acid 302 to about amino acid 305, from about amino acid 307 to about amino acid 310 and from about amino acid 376 to about amino acid 379, and amino acid sequence blocks having homology to myelin p0 protein from about amino acid 210 to about amino acid 239 and from about amino acid 92 to about amino acid 121. Clone DNA68872-1620 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203160.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 304 (SEQ ID NO:422), evidenced significant homology between the PRO1387 amino acid sequence and the following Dayhoff sequences: P\_W36955, MYP0\_HETFR, HS46KDA\_1, AF049498\_1, MYOO\_HUMAN, AF030454\_1, A53268, SHPTCRA\_1, P\_W14146 and GEN12838.

#### EXAMPLE 138: Isolation of cDNA clones Encoding Human PRO1384

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA54192. Based on the DNA54192 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1384.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TGCAGCCCCTGTGACACAACTGG-3' (SEQ ID NO:425)

reverse PCR primer 5'-CTGAGATAACCGAGCCATCCTCCCAC-3' (SEQ ID NO:426)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA54192 sequence which had the following nucleotide sequence:

hybridization probe

5'-GGAGATAGCTGCTATGGGTTCTTCAGGCACAACCTTAACATGGGAAG-3' (SEQ ID NO:427)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1384 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1384 (designated herein as DNA71159-1617 [Figure 305, SEQ ID NO:423]; and the derived protein sequence for PRO1384.

The entire coding sequence of PRO1384 is shown in Figure 305 (SEQ ID NO:423). Clone DNA71159-1617 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 182-184 and an apparent stop codon at nucleotide positions 869-871. The predicted polypeptide precursor is 229 amino acids long. The full-length PRO1384 protein shown in Figure 306 has an estimated molecular weight of about 26,650 daltons and a pI of about 8.76. Additional features include a type II

transmembrane domain at about amino acids 32-57, and potential N-glycosylation sites at about amino acids 68-71, 120-123, and 134-137.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 306 (SEQ ID NO:424), revealed homology between the PRO1384 amino acid sequence and the following Dayhoff sequences: AF054819\_1, HSAJ1687\_1, AF009511\_1, AB010710\_1, GEN13595, HSAJ673\_1, GEN13961, AB005900\_1, LECH\_CHICK, AF021349\_1, and NK13\_RAT.

Clone DNA71159-1617 has been deposited with ATCC and is assigned ATCC deposit no. 203135.

**EXAMPLE 139: Use of PRO as a hybridization probe**

The following method describes use of a nucleotide sequence encoding PRO as a hybridization probe.

DNA comprising the coding sequence of full-length or mature PRO as disclosed herein is employed as a probe to screen for homologous DNAs (such as those encoding naturally-occurring variants of PRO) in human tissue cDNA libraries or human tissue genomic libraries.

Hybridization and washing of filters containing either library DNAs is performed under the following high stringency conditions. Hybridization of radiolabeled PRO-derived probe to the filters is performed in a solution of 50% formamide, 5x SSC, 0.1% SDS, 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8, 2x Denhardt's solution, and 10% dextran sulfate at 42°C for 20 hours. Washing of the filters is performed in an aqueous solution of 0.1x SSC and 0.1% SDS at 42°C.

DNAs having a desired sequence identity with the DNA encoding full-length native sequence PRO can then be identified using standard techniques known in the art.

**EXAMPLE 140: Expression of PRO in *E. coli***

This example illustrates preparation of an unglycosylated form of PRO by recombinant expression in *E. coli*.

The DNA sequence encoding PRO is initially amplified using selected PCR primers. The primers should contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector. A variety of expression vectors may be employed. An example of a suitable vector is pBR322 (derived from *E. coli*; see Bolivar et al., Gene, 2:95 (1977)) which contains genes for ampicillin and tetracycline resistance. The vector is digested with restriction enzyme and dephosphorylated. The PCR amplified sequences are then ligated into the vector. The vector will preferably include sequences which encode for an antibiotic resistance gene, a trp promoter, a polyhis leader (including the first six STII codons, polyhis sequence, and enterokinase cleavage site), the PRO coding region, lambda transcriptional terminator, and an argU gene.

The ligation mixture is then used to transform a selected *E. coli* strain using the methods described in Sambrook et al., supra. Transformants are identified by their ability to grow on LB plates and antibiotic resistant colonies are then selected. Plasmid DNA can be isolated and confirmed by restriction analysis and DNA sequencing.



Selected clones can be grown overnight in liquid culture medium such as LB broth supplemented with antibiotics. The overnight culture may subsequently be used to inoculate a larger scale culture. The cells are then grown to a desired optical density, during which the expression promoter is turned on.

After culturing the cells for several more hours, the cells can be harvested by centrifugation. The cell pellet obtained by the centrifugation can be solubilized using various agents known in the art, and the solubilized PRO protein can then be purified using a metal chelating column under conditions that allow tight binding of the protein.

PRO may be expressed in *E. coli* in a poly-His tagged form, using the following procedure. The DNA encoding PRO is initially amplified using selected PCR primers. The primers will contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector, and other useful sequences providing for efficient and reliable translation initiation, rapid purification on a metal chelation column, and proteolytic removal with enterokinase. The PCR-amplified, poly-His tagged sequences are then ligated into an expression vector, which is used to transform an *E. coli* host based on strain 52 (W3110 fuhA(tonA) lon galE rpoHts(htpRts) clpP(lacIq). Transformants are first grown in LB containing 50 mg/ml carbenicillin at 30°C with shaking until an O.D.600 of 3-5 is reached. Cultures are then diluted 50-100 fold into CRAP media (prepared by mixing 3.57 g (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>, 0.71 g sodium citrate•2H<sub>2</sub>O, 1.07 g KCl, 5.36 g Difco yeast extract, 5.36 g Sheffield hycase SF in 500 mL water, as well as 110 mM MPOS, pH 7.3, 0.55 % (w/v) glucose and 7 mM MgSO<sub>4</sub>) and grown for approximately 20-30 hours at 30°C with shaking. Samples are removed to verify expression by SDS-PAGE analysis, and the bulk culture is centrifuged to pellet the cells. Cell pellets are frozen until purification and refolding.

*E. coli* paste from 0.5 to 1 L fermentations (6-10 g pellets) is resuspended in 10 volumes (w/v) in 7 M guanidine, 20 mM Tris, pH 8 buffer. Solid sodium sulfite and sodium tetrathionate is added to make final concentrations of 0.1M and 0.02 M, respectively, and the solution is stirred overnight at 4°C. This step results in a denatured protein with all cysteine residues blocked by sulfitolization. The solution is centrifuged at 40,000 rpm in a Beckman Ultracentrifuge for 30 min. The supernatant is diluted with 3-5 volumes of metal chelate column buffer (6 M guanidine, 20 mM Tris, pH 7.4) and filtered through 0.22 micron filters to clarify. The clarified extract is loaded onto a 5 ml Qiagen Ni-NTA metal chelate column equilibrated in the metal chelate column buffer. The column is washed with additional buffer containing 50 mM imidazole (Calbiochem, Utrol grade), pH 7.4. The protein is eluted with buffer containing 250 mM imidazole. Fractions containing the desired protein are pooled and stored at 4°C. Protein concentration is estimated by its absorbance at 280 nm using the calculated extinction coefficient based on its amino acid sequence.

The proteins are refolded by diluting the sample slowly into freshly prepared refolding buffer consisting of: 20 mM Tris, pH 8.6, 0.3 M NaCl, 2.5 M urea, 5 mM cysteine, 20 mM glycine and 1 mM EDTA. Refolding volumes are chosen so that the final protein concentration is between 50 to 100 micrograms/ml. The refolding solution is stirred gently at 4°C for 12-36 hours. The refolding reaction is quenched by the addition of TFA to a final concentration of 0.4% (pH of approximately 3). Before further purification of the protein, the solution is filtered through a 0.22 micron filter and acetonitrile is added to 2-10% final concentration. The refolded protein is chromatographed on a Poros R1/H reversed phase column

using a mobile buffer of 0.1 % TFA with elution with a gradient of acetonitrile from 10 to 80%. Aliquots of fractions with A280 absorbance are analyzed on SDS polyacrylamide gels and fractions containing homogeneous refolded protein are pooled. Generally, the properly refolded species of most proteins are eluted at the lowest concentrations of acetonitrile since those species are the most compact with their hydrophobic interiors shielded from interaction with the reversed phase resin. Aggregated species are usually eluted at higher acetonitrile concentrations. In addition to resolving misfolded forms of proteins from the desired form, the reversed phase step also removes endotoxin from the samples.

Fractions containing the desired folded PRO polypeptide are pooled and the acetonitrile removed using a gentle stream of nitrogen directed at the solution. Proteins are formulated into 20 mM Hepes, pH 6.8 with 0.14 M sodium chloride and 4% mannitol by dialysis or by gel filtration using G25 Superfine (Pharmacia) resins equilibrated in the formulation buffer and sterile filtered.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### EXAMPLE 141: Expression of PRO in mammalian cells

This example illustrates preparation of a potentially glycosylated form of PRO by recombinant expression in mammalian cells.

The vector, pRK5 (see EP 307,247, published March 15, 1989), is employed as the expression vector. Optionally, the PRO DNA is ligated into pRK5 with selected restriction enzymes to allow insertion of the PRO DNA using ligation methods such as described in Sambrook et al., *supra*. The resulting vector is called pRK5-PRO.

In one embodiment, the selected host cells may be 293 cells. Human 293 cells (ATCC CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, nutrient components and/or antibiotics. About 10  $\mu$ g pRK5-PRO DNA is mixed with about 1  $\mu$ g DNA encoding the VA RNA gene [Thimmappaya et al., *Cell*, 31:543 (1982)] and dissolved in 500  $\mu$ l of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M  $\text{CaCl}_2$ . To this mixture is added, dropwise, 500  $\mu$ l of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM  $\text{NaPO}_4$ , and a precipitate is allowed to form for 10 minutes at 25°C. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37°C. The culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

Approximately 24 hours after the transfections, the culture medium is removed and replaced with culture medium (alone) or culture medium containing 200  $\mu$ Ci/ml  $^{35}\text{S}$ -cysteine and 200  $\mu$ Ci/ml  $^{35}\text{S}$ -methionine. After a 12 hour incubation, the conditioned medium is collected, concentrated on a spin filter, and loaded onto a 15% SDS gel. The processed gel may be dried and exposed to film for a selected period of time to reveal the presence of PRO polypeptide. The cultures containing transfected cells may undergo further incubation (in serum free medium) and the medium is tested in selected bioassays.

In an alternative technique, PRO may be introduced into 293 cells transiently using the dextran sulfate method described by Sompayrac et al., *Proc. Natl. Acad. Sci.*, 12:7575 (1981). 293 cells are grown to

maximal density in a spinner flask and 700  $\mu$ g pRK5-PRO DNA is added. The cells are first concentrated from the spinner flask by centrifugation and washed with PBS. The DNA-dextran precipitate is incubated on the cell pellet for four hours. The cells are treated with 20% glycerol for 90 seconds, washed with tissue culture medium, and re-introduced into the spinner flask containing tissue culture medium, 5  $\mu$ g/ml bovine insulin and 0.1  $\mu$ g/ml bovine transferrin. After about four days, the conditioned media is centrifuged and filtered to remove cells and debris. The sample containing expressed PRO can then be concentrated and purified by any selected method, such as dialysis and/or column chromatography.

In another embodiment, PRO can be expressed in CHO cells. The pRK5-PRO can be transfected into CHO cells using known reagents such as  $\text{CaPO}_4$  or DEAE-dextran. As described above, the cell cultures can be incubated, and the medium replaced with culture medium (alone) or medium containing a radiolabel such as  $^{35}\text{S}$ -methionine. After determining the presence of PRO polypeptide, the culture medium may be replaced with serum free medium. Preferably, the cultures are incubated for about 6 days, and then the conditioned medium is harvested. The medium containing the expressed PRO can then be concentrated and purified by any selected method.

Epitope-tagged PRO may also be expressed in host CHO cells. The PRO may be subcloned out of the pRK5 vector. The subclone insert can undergo PCR to fuse in frame with a selected epitope tag such as a poly-his tag into a Baculovirus expression vector. The poly-his tagged PRO insert can then be subcloned into a SV40 driven vector containing a selection marker such as DHFR for selection of stable clones. Finally, the CHO cells can be transfected (as described above) with the SV40 driven vector. Labeling may be performed, as described above, to verify expression. The culture medium containing the expressed poly-His tagged PRO can then be concentrated and purified by any selected method, such as by  $\text{Ni}^{2+}$ -chelate affinity chromatography.

PRO may also be expressed in CHO and/or COS cells by a transient expression procedure or in CHO cells by another stable expression procedure.

Stable expression in CHO cells is performed using the following procedure. The proteins are expressed as an IgG construct (immunoadhesin), in which the coding sequences for the soluble forms (e.g. extracellular domains) of the respective proteins are fused to an IgG1 constant region sequence containing the hinge, CH2 and CH2 domains and/or is a poly-His tagged form.

Following PCR amplification, the respective DNAs are subcloned in a CHO expression vector using standard techniques as described in Ausubel et al., Current Protocols of Molecular Biology, Unit 3.16, John Wiley and Sons (1997). CHO expression vectors are constructed to have compatible restriction sites 5' and 3' of the DNA of interest to allow the convenient shuttling of cDNA's. The vector used expression in CHO cells is as described in Lucas et al., Nucl. Acids Res. 24:9 (1774-1779 (1996), and uses the SV40 early promoter/enhancer to drive expression of the cDNA of interest and dihydrofolate reductase (DHFR). DHFR expression permits selection for stable maintenance of the plasmid following transfection.

Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect<sup>®</sup> (Quiagen), Dosper<sup>®</sup> or Fugene<sup>®</sup> (Boehringer Mannheim). The cells are grown as described in Lucas et al., supra. Approximately  $3 \times 10^7$  cells are frozen

in an ampule for further growth and production as described below.

The ampules containing the plasmid DNA are thawed by placement into water bath and mixed by vortexing. The contents are pipetted into a centrifuge tube containing 10 mLs of media and centrifuged at 1000 rpm for 5 minutes. The supernatant is aspirated and the cells are resuspended in 10 mL of selective media (0.2  $\mu$ m filtered PS20 with 5% 0.2  $\mu$ m diafiltered fetal bovine serum). The cells are then aliquoted into a 100 mL spinner containing 90 mL of selective media. After 1-2 days, the cells are transferred into a 250 mL spinner filled with 150 mL selective growth medium and incubated at 37°C. After another 2-3 days, 250 mL, 500 mL and 2000 mL spinners are seeded with  $3 \times 10^5$  cells/mL. The cell media is exchanged with fresh media by centrifugation and resuspension in production medium. Although any suitable CHO media may be employed, a production medium described in U.S. Patent No. 5,122,469, issued June 16, 1992 may actually be used. A 3L production spinner is seeded at  $1.2 \times 10^6$  cells/mL. On day 0, the cell number pH is determined. On day 1, the spinner is sampled and sparging with filtered air is commenced. On day 2, the spinner is sampled, the temperature shifted to 33°C, and 30 mL of 500 g/L glucose and 0.6 mL of 10% antifoam (e.g., 35% polydimethylsiloxane emulsion, Dow Corning 365 Medical Grade Emulsion) taken. Throughout the production, the pH is adjusted as necessary to keep it at around 7.2. After 10 days, or until the viability dropped below 70%, the cell culture is harvested by centrifugation and filtering through a 0.22  $\mu$ m filter. The filtrate was either stored at 4°C or immediately loaded onto columns for purification.

For the poly-His tagged constructs, the proteins are purified using a Ni-NTA column (Qiagen). Before purification, imidazole is added to the conditioned media to a concentration of 5 mM. The conditioned media is pumped onto a 6 ml Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 M NaCl and 5 mM imidazole at a flow rate of 4-5 ml/min. at 4°C. After loading, the column is washed with additional equilibration buffer and the protein eluted with equilibration buffer containing 0.25 M imidazole. The highly purified protein is subsequently desalted into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 ml G25 Superfine (Pharmacia) column and stored at -80°C.

Immunoadhesin (Fc-containing) constructs are purified from the conditioned media as follows. The conditioned medium is pumped onto a 5 ml Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column is washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein is immediately neutralized by collecting 1 ml fractions into tubes containing 275  $\mu$ L of 1 M Tris buffer, pH 9. The highly purified protein is subsequently desalted into storage buffer as described above for the poly-His tagged proteins. The homogeneity is assessed by SDS polyacrylamide gels and by N-terminal amino acid sequencing by Edman degradation.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### EXAMPLE 142: Expression of PRO in Yeast

The following method describes recombinant expression of PRO in yeast.

First, yeast expression vectors are constructed for intracellular production or secretion of PRO from the ADH2/GAPDH promoter. DNA encoding PRO and the promoter is inserted into suitable restriction enzyme sites in the selected plasmid to direct intracellular expression of PRO. For secretion, DNA encoding

PRO can be cloned into the selected plasmid, together with DNA encoding the ADH2/GAPDH promoter, a native PRO signal peptide or other mammalian signal peptide, or, for example, a yeast alpha-factor or invertase secretory signal/leader sequence, and linker sequences (if needed) for expression of PRO.

Yeast cells, such as yeast strain AB110, can then be transformed with the expression plasmids described above and cultured in selected fermentation media. The transformed yeast supernatants can be analyzed by precipitation with 10% trichloroacetic acid and separation by SDS-PAGE, followed by staining of the gels with Coomassie Blue stain.

Recombinant PRO can subsequently be isolated and purified by removing the yeast cells from the fermentation medium by centrifugation and then concentrating the medium using selected cartridge filters. The concentrate containing PRO may further be purified using selected column chromatography resins.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### EXAMPLE 143: Expression of PRO in Baculovirus-Infected Insect Cells

The following method describes recombinant expression of PRO in Baculovirus-infected insect cells.

The sequence coding for PRO is fused upstream of an epitope tag contained within a baculovirus expression vector. Such epitope tags include poly-his tags and immunoglobulin tags (like Fc regions of IgG). A variety of plasmids may be employed, including plasmids derived from commercially available plasmids such as pVL1393 (Novagen). Briefly, the sequence encoding PRO or the desired portion of the coding sequence of PRO such as the sequence encoding the extracellular domain of a transmembrane protein or the sequence encoding the mature protein if the protein is extracellular is amplified by PCR with primers complementary to the 5' and 3' regions. The 5' primer may incorporate flanking (selected) restriction enzyme sites. The product is then digested with those selected restriction enzymes and subcloned into the expression vector.

Recombinant baculovirus is generated by co-transfecting the above plasmid and BaculoGold™ virus DNA (Pharmingen) into *Spodoptera frugiperda* ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL). After 4 - 5 days of incubation at 28°C, the released viruses are harvested and used for further amplifications. Viral infection and protein expression are performed as described by O'Reilley et al., Baculovirus expression vectors: A Laboratory Manual, Oxford: Oxford University Press (1994).

Expressed poly-his tagged PRO can then be purified, for example, by Ni<sup>2+</sup>-chelate affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by Rupert et al., Nature, 362:175-179 (1993). Briefly, Sf9 cells are washed, resuspended in sonication buffer (25 mL Hepes, pH 7.9; 12.5 mM MgCl<sub>2</sub>; 0.1 mM EDTA; 10% glycerol; 0.1% NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the supernatant is diluted 50-fold in loading buffer (50 mM phosphate, 300 mM NaCl, 10% glycerol, pH 7.8) and filtered through a 0.45 μm filter. A Ni<sup>2+</sup>-NTA agarose column (commercially available from Qiagen) is prepared with a bed volume of 5 mL, washed with 25 mL of water and equilibrated with 25 mL of loading buffer. The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed to baseline A<sub>280</sub> with loading buffer, at which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50 mM phosphate; 300 mM NaCl, 10% glycerol, pH 6.0), which elutes nonspecifically bound

protein. After reaching  $A_{280}$  baseline again, the column is developed with a 0 to 500 mM Imidazole gradient in the secondary wash buffer. One mL fractions are collected and analyzed by SDS-PAGE and silver staining or Western blot with  $Ni^{2+}$ -NTA-conjugated to alkaline phosphatase (Qiagen). Fractions containing the eluted His<sub>10</sub>-tagged PRO are pooled and dialyzed against loading buffer.

Alternatively, purification of the IgG tagged (or Fc tagged) PRO can be performed using known chromatography techniques, including for instance, Protein A or protein G column chromatography.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### EXAMPLE 144: Preparation of Antibodies that Bind PRO

This example illustrates preparation of monoclonal antibodies which can specifically bind PRO.

Techniques for producing the monoclonal antibodies are known in the art and are described, for instance, in Goding, supra. Immunogens that may be employed include purified PRO, fusion proteins containing PRO, and cells expressing recombinant PRO on the cell surface. Selection of the immunogen can be made by the skilled artisan without undue experimentation.

Mice, such as Balb/c, are immunized with the PRO immunogen emulsified in complete Freund's adjuvant and injected subcutaneously or intraperitoneally in an amount from 1-100 micrograms. Alternatively, the immunogen is emulsified in MPL-TDM adjuvant (Ribi Immunochemical Research, Hamilton, MT) and injected into the animal's hind foot pads. The immunized mice are then boosted 10 to 12 days later with additional immunogen emulsified in the selected adjuvant. Thereafter, for several weeks, the mice may also be boosted with additional immunization injections. Serum samples may be periodically obtained from the mice by retro-orbital bleeding for testing in ELISA assays to detect anti-PRO antibodies.

After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a final intravenous injection of PRO. Three to four days later, the mice are sacrificed and the spleen cells are harvested. The spleen cells are then fused (using 35% polyethylene glycol) to a selected murine myeloma cell line such as P3X63AgU.1, available from ATCC, No. CRL 1597. The fusions generate hybridoma cells which can then be plated in 96 well tissue culture plates containing HAT (hypoxanthine, aminopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids, and spleen cell hybrids.

The hybridoma cells will be screened in an ELISA for reactivity against PRO. Determination of "positive" hybridoma cells secreting the desired monoclonal antibodies against PRO is within the skill in the art.

The positive hybridoma cells can be injected intraperitoneally into syngeneic Balb/c mice to produce ascites containing the anti-PRO monoclonal antibodies. Alternatively, the hybridoma cells can be grown in tissue culture flasks or roller bottles. Purification of the monoclonal antibodies produced in the ascites can be accomplished using ammonium sulfate precipitation, followed by gel exclusion chromatography. Alternatively, affinity chromatography based upon binding of antibody to protein A or protein G can be employed.

#### EXAMPLE 145: Purification of PRO Polypeptides Using Specific Antibodies

Native or recombinant PRO polypeptides may be purified by a variety of standard techniques in the

art of protein purification. For example, pro-PRO polypeptide, mature PRO polypeptide, or pre-PRO polypeptide is purified by immunoaffinity chromatography using antibodies specific for the PRO polypeptide of interest. In general, an immunoaffinity column is constructed by covalently coupling the anti-PRO polypeptide antibody to an activated chromatographic resin.

5 Polyclonal immunoglobulins are prepared from immune sera either by precipitation with ammonium sulfate or by purification on immobilized Protein A (Pharmacia LKB Biotechnology, Piscataway, N.J.). Likewise, monoclonal antibodies are prepared from mouse ascites fluid by ammonium sulfate precipitation or chromatography on immobilized Protein A. Partially purified immunoglobulin is covalently attached to a chromatographic resin such as CnBr-activated SEPHAROSE™ (Pharmacia LKB Biotechnology). The antibody is coupled to the resin, the resin is blocked, and the derivative resin is washed according to the manufacturer's instructions.

10 Such an immunoaffinity column is utilized in the purification of PRO polypeptide by preparing a fraction from cells containing PRO polypeptide in a soluble form. This preparation is derived by solubilization of the whole cell or of a subcellular fraction obtained via differential centrifugation by the addition of detergent or by other methods well known in the art. Alternatively, soluble PRO polypeptide containing a signal sequence may be secreted in useful quantity into the medium in which the cells are grown.

15 A soluble PRO polypeptide-containing preparation is passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of PRO polypeptide (*e.g.*, high ionic strength buffers in the presence of detergent). Then, the column is eluted under conditions that disrupt antibody/PRO polypeptide binding (*e.g.*, a low pH buffer such as approximately pH 2-3, or a high concentration of a chaotrope such as urea or thiocyanate ion), and PRO polypeptide is collected.

#### EXAMPLE 146: Drug Screening

25 This invention is particularly useful for screening compounds by using PRO polypeptides or binding fragment thereof in any of a variety of drug screening techniques. The PRO polypeptide or fragment employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the PRO polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between PRO polypeptide or a fragment and the agent being tested. Alternatively, one can examine the diminution in complex formation between the PRO polypeptide and its target cell or target receptors caused by the agent being tested.

30 Thus, the present invention provides methods of screening for drugs or any other agents which can affect a PRO polypeptide-associated disease or disorder. These methods comprise contacting such an agent with an PRO polypeptide or fragment thereof and assaying (i) for the presence of a complex between the agent and the PRO polypeptide or fragment, or (ii) for the presence of a complex between the PRO polypeptide or fragment and the cell, by methods well known in the art. In such competitive binding assays, the PRO polypeptide or fragment is typically labeled. After suitable incubation, free PRO polypeptide or fragment is

separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of the particular agent to bind to PRO polypeptide or to interfere with the PRO polypeptide/cell complex.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to a polypeptide and is described in detail in WO 84/03564, published on September 13, 1984. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. As applied to a PRO polypeptide, the peptide test compounds are reacted with PRO polypeptide and washed. Bound PRO polypeptide is detected by methods well known in the art. Purified PRO polypeptide can also be coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the peptide and immobilize it on the solid support.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding PRO polypeptide specifically compete with a test compound for binding to PRO polypeptide or fragments thereof. In this manner, the antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with PRO polypeptide.

#### EXAMPLE 147: Rational Drug Design

The goal of rational drug design is to produce structural analogs of biologically active polypeptide of interest (*i.e.*, a PRO polypeptide) or of small molecules with which they interact, *e.g.*, agonists, antagonists, or inhibitors. Any of these examples can be used to fashion drugs which are more active or stable forms of the PRO polypeptide or which enhance or interfere with the function of the PRO polypeptide *in vivo* (*c.f.*, Hodgson, Bio/Technology, 9: 19-21 (1991)).

In one approach, the three-dimensional structure of the PRO polypeptide, or of an PRO polypeptide-inhibitor complex, is determined by x-ray crystallography, by computer modeling or, most typically, by a combination of the two approaches. Both the shape and charges of the PRO polypeptide must be ascertained to elucidate the structure and to determine active site(s) of the molecule. Less often, useful information regarding the structure of the PRO polypeptide may be gained by modeling based on the structure of homologous proteins. In both cases, relevant structural information is used to design analogous PRO polypeptide-like molecules or to identify efficient inhibitors. Useful examples of rational drug design may include molecules which have improved activity or stability as shown by Braxton and Wells, Biochemistry, 31:7796-7801 (1992) or which act as inhibitors, agonists, or antagonists of native peptides as shown by Athauda *et al.*, J. Biochem., 113:742-746 (1993).

It is also possible to isolate a target-specific antibody, selected by functional assay, as described above, and then to solve its crystal structure. This approach, in principle, yields a pharmacore upon which subsequent drug design can be based. It is possible to bypass protein crystallography altogether by generating anti-idiotypic antibodies (anti-ids) to a functional, pharmacologically active antibody. As a mirror image of a mirror image, the binding site of the anti-ids would be expected to be an analog of the original receptor. The anti-id could then be used to identify and isolate peptides from banks of chemically or biologically produced



peptides. The isolated peptides would then act as the pharmacore.

By virtue of the present invention, sufficient amounts of the PRO polypeptide may be made available to perform such analytical studies as X-ray crystallography. In addition, knowledge of the PRO polypeptide amino acid sequence provided herein will provide guidance to those employing computer modeling techniques in place of or in addition to x-ray crystallography.

**EXAMPLE 148: Stimulation of Heart Neonatal Hypertrophy (Assay 1)**

This assay is designed to measure the ability of PRO polypeptides to stimulate hypertrophy of neonatal heart. PRO polypeptides testing positive in this assay are expected to be useful for the therapeutic treatment of various cardiac insufficiency disorders.

Cardiac myocytes from 1-day old Harlan Sprague Dawley rats were obtained. Cells ( $180\ \mu\text{l}$  at  $7.5 \times 10^4/\text{ml}$ , serum  $<0.1\%$ , freshly isolated) are added on day 1 to 96-well plates previously coated with DMEM/F12 + 4% FCS. Test samples containing the test PRO polypeptide or growth medium only (negative control) ( $20\ \mu\text{l}/\text{well}$ ) are added directly to the wells on day 1. PGF ( $20\ \mu\text{l}/\text{well}$ ) is then added on day 2 at final concentration of  $10^{-6}\ \text{M}$ . The cells are then stained on day 4 and visually scored on day 5, wherein cells showing no increase in size as compared to negative controls are scored 0.0, cells showing a small to moderate increase in size as compared to negative controls are scored 1.0 and cells showing a large increase in size as compared to negative controls are scored 2.0. A positive result in the assay is a score of 1.0 or greater.

The following polypeptides tested positive in this assay: PRO1312.

**EXAMPLE 149: Stimulation of Endothelial Cell Proliferation (Assay 8)**

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to stimulate adrenal cortical capillary endothelial cell (ACE) growth. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of conditions or disorders where angiogenesis would be beneficial including, for example, wound healing, and the like (as would agonists of these PRO polypeptides). Antagonists of the PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of cancerous tumors.

Bovine adrenal cortical capillary endothelial (ACE) cells (from primary culture, maximum of 12-14 passages) were plated in 96-well plates at 500 cells/well per 100 microliter. Assay media included low glucose DMEM, 10% calf serum, 2 mM glutamine, and 1X penicillin/streptomycin/fungizone. Control wells included the following: (1) no ACE cells added; (2) ACE cells alone; (3) ACE cells plus VEGF (5 ng/ml); and (4) ACE cells plus FGF (5ng/ml). The control or test sample, (in 100 microliter volumes), was then added to the wells (at dilutions of 1%, 0.1% and 0.01%, respectively). The cell cultures were incubated for 6-7 days at  $37^\circ\text{C}/5\%\ \text{CO}_2$ . After the incubation, the media in the wells was aspirated, and the cells were washed 1X with PBS. An acid phosphatase reaction mixture (100 microliter; 0.1M sodium acetate, pH 5.5, 0.1% Triton X-100, 10 mM p-nitrophenyl phosphate) was then added to each well. After a 2 hour incubation at  $37^\circ\text{C}$ , the reaction was stopped by addition of 10 microliters 1N NaOH. Optical density (OD) was measured on a microplate reader at 405 nm.

The activity of a PRO polypeptide was calculated as the fold increase in proliferation (as determined by the acid phosphatase activity, OD 405 nm) relative to (1) cell only background, and (2) relative to maximum stimulation by VEGF. VEGF (at 3-10 ng/ml) and FGF (at 1-5 ng/ml) were employed as an activity reference for maximum stimulation. Results of the assay were considered "positive" if the observed stimulation was  $\geq$  50% increase over background. VEGF (5 ng/ml) control at 1% dilution gave 1.24 fold stimulation; FGF (5 ng/ml) control at 1% dilution gave 1.46 fold stimulation.

The following PRO polypeptides tested positive in this assay: PRO1154 and PRO1186.

**EXAMPLE 150: Inhibition of Vascular Endothelial Growth Factor (VEGF) Stimulated Proliferation of Endothelial Cell Growth (Assay 9)**

The ability of various PRO polypeptides to inhibit VEGF stimulated proliferation of endothelial cells was tested. Polypeptides testing positive in this assay are useful for inhibiting endothelial cell growth in mammals where such an effect would be beneficial, e.g., for inhibiting tumor growth.

Specifically, bovine adrenal cortical capillary endothelial cells (ACE) (from primary culture, maximum of 12-14 passages) were plated in 96-well plates at 500 cells/well per 100 microliter. Assay media included low glucose DMEM, 10% calf serum, 2 mM glutamine, and 1X penicillin/streptomycin/fungizone. Control wells included the following: (1) no ACE cells added; (2) ACE cells alone; (3) ACE cells plus 5 ng/ml FGF; (4) ACE cells plus 3 ng/ml VEGF; (5) ACE cells plus 3 ng/ml VEGF plus 1 ng/ml TGF-beta; and (6) ACE cells plus 3 ng/ml VEGF plus 5 ng/ml LIF. The test samples, poly-his tagged PRO polypeptides (in 100 microliter volumes), were then added to the wells (at dilutions of 1%, 0.1% and 0.01%, respectively). The cell cultures were incubated for 6-7 days at 37°C/5% CO<sub>2</sub>. After the incubation, the media in the wells was aspirated, and the cells were washed 1X with PBS. An acid phosphatase reaction mixture (100 microliter; 0.1M sodium acetate, pH 5.5, 0.1% Triton X-100, 10 mM p-nitrophenyl phosphate) was then added to each well. After a 2 hour incubation at 37°C, the reaction was stopped by addition of 10 microliters 1N NaOH. Optical density (OD) was measured on a microplate reader at 405 nm.

The activity of PRO polypeptides was calculated as the percent inhibition of VEGF (3 ng/ml) stimulated proliferation (as determined by measuring acid phosphatase activity at OD 405 nm) relative to the cells without stimulation. TGF-beta was employed as an activity reference at 1 ng/ml, since TGF-beta blocks 70-90% of VEGF-stimulated ACE cell proliferation. The results are indicative of the utility of the PRO polypeptides in cancer therapy and specifically in inhibiting tumor angiogenesis. Numerical values (relative inhibition) are determined by calculating the percent inhibition of VEGF stimulated proliferation by the PRO polypeptides relative to cells without stimulation and then dividing that percentage into the percent inhibition obtained by TGF- $\beta$  at 1 ng/ml which is known to block 70-90% of VEGF stimulated cell proliferation. The results are considered positive if the PRO polypeptide exhibits 30% or greater inhibition of VEGF stimulation of endothelial cell growth (relative inhibition 30% or greater).

The following polypeptide tested positive in this assay: PRO812.

**EXAMPLE 151: Stimulatory Activity in Mixed Lymphocyte Reaction (MLR) Assay (Assay 24)**

This example shows that certain polypeptides of the invention are active as a stimulator of the proliferation of stimulated T-lymphocytes. Compounds which stimulate proliferation of lymphocytes are useful therapeutically where enhancement of an immune response is beneficial. A therapeutic agent may take the form of antagonists of the polypeptide of the invention, for example, murine-human chimeric, humanized or human antibodies against the polypeptide.

The basic protocol for this assay is described in Current Protocols in Immunology, unit 3.12; edited by J E Coligan, A M Kruisbeek, D H Marglies, E M Shevach, W Strober, National Institutes of Health, Published by John Wiley & Sons, Inc.

More specifically, in one assay variant, peripheral blood mononuclear cells (PBMC) are isolated from mammalian individuals, for example a human volunteer, by leukopheresis (one donor will supply stimulator PBMCs, the other donor will supply responder PBMCs). If desired, the cells are frozen in fetal bovine serum and DMSO after isolation. Frozen cells may be thawed overnight in assay media (37°C, 5% CO<sub>2</sub>) and then washed and resuspended to 3x10<sup>6</sup> cells/ml of assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate). The stimulator PBMCs are prepared by irradiating the cells (about 3000 Rads).

The assay is prepared by plating in triplicate wells a mixture of:

100:1 of test sample diluted to 1% or to 0.1%,

50 :1 of irradiated stimulator cells, and

50 :1 of responder PBMC cells.

100 microliters of cell culture media or 100 microliter of CD4-IgG is used as the control. The wells are then incubated at 37°C, 5% CO<sub>2</sub> for 4 days. On day 5, each well is pulsed with tritiated thymidine (1.0 mCi/well; Amersham). After 6 hours the cells are washed 3 times and then the uptake of the label is evaluated.

In another variant of this assay, PBMCs are isolated from the spleens of Balb/c mice and C57B6 mice. The cells are teased from freshly harvested spleens in assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate) and the PBMCs are isolated by overlaying these cells over Lympholyte M (Organon Teknika), centrifuging at 2000 rpm for 20 minutes, collecting and washing the mononuclear cell layer in assay media and resuspending the cells to 1x10<sup>7</sup> cells/ml of assay media. The assay is then conducted as described above.

Positive increases over control are considered positive with increases of greater than or equal to 180% being preferred. However, any value greater than control indicates a stimulatory effect for the test protein.

The following PRO polypeptides tested positive in this assay: PRO826, PRO1068, PRO1184, PRO1346 and PRO1375.

**EXAMPLE 152: Retinal Neuron Survival (Assay 52)**

This example demonstrates that certain PRO polypeptides have efficacy in enhancing the survival of retinal neuron cells and, therefore, are useful for the therapeutic treatment of retinal disorders or injuries including, for example, treating sight loss in mammals due to retinitis pigmentosum, AMD, etc.

Sprague Dawley rat pups at postnatal day 7 (mixed population: glia and retinal neuronal types) are killed by decapitation following CO<sub>2</sub> anesthesia and the eyes are removed under sterile conditions. The neural retina is dissected away from the pigment epithelium and other ocular tissue and then dissociated into a single cell suspension using 0.25 % trypsin in Ca<sup>2+</sup>, Mg<sup>2+</sup>-free PBS. The retinas are incubated at 37°C for 7-10 minutes after which the trypsin is inactivated by adding 1 ml soybean trypsin inhibitor. The cells are plated at 100,000 cells per well in 96 well plates in DMEM/F12 supplemented with N2 and with or without the specific test PRO polypeptide. Cells for all experiments are grown at 37°C in a water saturated atmosphere of 5% CO<sub>2</sub>. After 2-3 days in culture, cells are stained with calcein AM then fixed using 4% paraformaldehyde and stained with DAPI for determination of total cell count. The total cells (fluorescent) are quantified at 20X objective magnification using CCD camera and NIH image software for MacIntosh. Fields in the well are chosen at random.

The effect of various concentration of PRO polypeptides are reported herein where percent survival is calculated by dividing the total number of calcein AM positive cells at 2-3 days in culture by the total number of DAPI-labeled cells at 2-3 days in culture. Anything above 30% survival is considered positive.

The following PRO polypeptides tested positive in this assay using polypeptide concentrations within the range of 0.01 % to 1.0% in the assay: PRO828, PRO826, PRO1068 and PRO1132.

#### EXAMPLE 153: Rod Photoreceptor Cell Survival (Assay 56)

This assay shows that certain polypeptides of the invention act to enhance the survival/proliferation of rod photoreceptor cells and, therefore, are useful for the therapeutic treatment of retinal disorders or injuries including, for example, treating sight loss in mammals due to retinitis pigmentosum, AMD, etc.

Sprague Dawley rat pups at 7 day postnatal (mixed population: glia and retinal neuronal cell types) are killed by decapitation following CO<sub>2</sub> anesthesia and the eyes are removed under sterile conditions. The neural retina is dissected away from the pigment epithelium and other ocular tissue and then dissociated into a single cell suspension using 0.25 % trypsin in Ca<sup>2+</sup>, Mg<sup>2+</sup>-free PBS. The retinas are incubated at 37°C for 7-10 minutes after which the trypsin is inactivated by adding 1 ml soybean trypsin inhibitor. The cells are plated at 100,000 cells per well in 96 well plates in DMEM/F12 supplemented with N<sub>2</sub>. Cells for all experiments are grown at 37°C in a water saturated atmosphere of 5% CO<sub>2</sub>. After 2-3 days in culture, cells are fixed using 4% paraformaldehyde, and then stained using CellTracker Green CMFDA. Rho 4D2 (ascites or IgG 1:100), a monoclonal antibody directed towards the visual pigment rhodopsin is used to detect rod photoreceptor cells by indirect immunofluorescence. The results are calculated as % survival: total number of calcein - rhodopsin positive cells at 2-3 days in culture, divided by the total number of rhodopsin positive cells at time 2-3 days in culture. The total cells (fluorescent) are quantified at 20x objective magnification using a CCD camera and NIH image software for MacIntosh. Fields in the well are chosen at random.

The following polypeptides tested positive in this assay: PRO536, PRO943, PRO828, PRO826, PRO1068 and PRO1132.

**EXAMPLE 154: Induction of c-fos in Endothelial Cells (Assay 34)**

This assay is designed to determine whether PRO polypeptides show the ability to induce c-fos in endothelial cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of conditions or disorders where angiogenesis would be beneficial including, for example, wound healing, and the like (as would agonists of these PRO polypeptides). Antagonists of the PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of cancerous tumors.

Human venous umbilical vein endothelial cells (HUVEC, Cell Systems) in growth media (50% Ham's F12 w/o GHT: low glucose, and 50% DMEM without glycine: with NaHCO<sub>3</sub>, 1% glutamine, 10 mM HEPES, 10% FBS, 10 ng/ml bFGF) were plated on 96-well microtiter plates at a cell density of 1x10<sup>4</sup> cells/well. The day after plating, the cells were starved by removing the growth media and treating the cells with 100 µl/well test samples and controls (positive control = growth media; negative control = Protein 32 buffer = 10 mM HEPES, 140 mM NaCl, 4% (w/v) mannitol, pH 6.8). The cells were incubated for 30 minutes at 37°C, in 5% CO<sub>2</sub>. The samples were removed, and the first part of the bDNA kit protocol (Chiron Diagnostics, cat. #6005-037) was followed, where each capitalized reagent/buffer listed below was available from the kit.

Briefly, the amounts of the TM Lysis Buffer and Probes needed for the tests were calculated based on information provided by the manufacturer. The appropriate amounts of thawed Probes were added to the TM Lysis Buffer. The Capture Hybridization Buffer was warmed to room temperature. The bDNA strips were set up in the metal strip holders, and 100 µl of Capture Hybridization Buffer was added to each b-DNA well needed, followed by incubation for at least 30 minutes. The test plates with the cells were removed from the incubator, and the media was gently removed using the vacuum manifold. 100 µl of Lysis Hybridization Buffer with Probes were quickly pipetted into each well of the microtiter plates. The plates were then incubated at 55°C for 15 minutes. Upon removal from the incubator, the plates were placed on the vortex mixer with the microtiter adapter head and vortexed on the #2 setting for one minute. 80 µl of the lysate was removed and added to the bDNA wells containing the Capture Hybridization Buffer, and pipetted up and down to mix. The plates were incubated at 53°C for at least 16 hours.

On the next day, the second part of the bDNA kit protocol was followed. Specifically, the plates were removed from the incubator and placed on the bench to cool for 10 minutes. The volumes of additions needed were calculated based upon information provided by the manufacturer. An Amplifier Working Solution was prepared by making a 1:100 dilution of the Amplifier Concentrate (20 fm/µl) in AL Hybridization Buffer. The hybridization mixture was removed from the plates and washed twice with Wash A. 50 µl of Amplifier Working Solution was added to each well and the wells were incubated at 53°C for 30 minutes. The plates were then removed from the incubator and allowed to cool for 10 minutes. The Label Probe Working Solution was prepared by making a 1:100 dilution of Label Concentrate (40 pmoles/µl) in AL Hybridization Buffer. After the 10-minute cool-down period, the amplifier hybridization mixture was removed and the plates were washed twice with Wash A. 50 µl of Label Probe Working Solution was added to each well and the wells were incubated at 53°C for 15 minutes. After cooling for 10 minutes, the Substrate was warmed to room

temperature. Upon addition of 3  $\mu$ l of Substrate Enhancer to each ml of Substrate needed for the assay, the plates were allowed to cool for 10 minutes, the label hybridization mixture was removed, and the plates were washed twice with Wash A and three times with Wash D. 50  $\mu$ l of the Substrate Solution with Enhancer was added to each well. The plates were incubated for 30 minutes at 37°C and RLU was read in an appropriate luminometer.

5           The replicates were averaged and the coefficient of variation was determined. The measure of activity of the fold increase over the negative control (Protein 32/HEPES buffer described above) value was indicated by chemiluminescence units (RLU). The results are considered positive if the PRO polypeptide exhibits at least a two-fold value over the negative buffer control. Negative control = 1.00 RLU at 1.00% dilution. Positive control = 8.39 RLU at 1.00% dilution.

10           The following PRO polypeptides tested positive in this assay: PRO535, PRO826, PRO819, PRO1126, PRO1160 and PRO1387.

EXAMPLE 155: Inhibitory Activity in Mixed Lymphocyte Reaction (MLR) Assay (Assay 67)

15           This example shows that one or more of the polypeptides of the invention are active as inhibitors of the proliferation of stimulated T-lymphocytes. Compounds which inhibit proliferation of lymphocytes are useful therapeutically where suppression of an immune response is beneficial.

          The basic protocol for this assay is described in Current Protocols in Immunology, unit 3.12; edited by J E Coligan, A M Kruisbeek, D H Marglies, E M Shevach, W Strober, National Institutes of Health, Published by John Wiley & Sons, Inc.

20           More specifically, in one assay variant, peripheral blood mononuclear cells (PBMC) are isolated from mammalian individuals, for example a human volunteer, by leukopheresis (one donor will supply stimulator PBMCs, the other donor will supply responder PBMCs). If desired, the cells are frozen in fetal bovine serum and DMSO after isolation. Frozen cells may be thawed overnight in assay media (37°C, 5% CO<sub>2</sub>) and then washed and resuspended to 3x10<sup>6</sup> cells/ml of assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate). The stimulator PBMCs are prepared by irradiating the cells (about 3000 Rads).

          The assay is prepared by plating in triplicate wells a mixture of:

100:1 of test sample diluted to 1% or to 0.1%,

50 :1 of irradiated stimulator cells, and

30           50 :1 of responder PBMC cells.

100 microliters of cell culture media or 100 microliter of CD4-IgG is used as the control. The wells are then incubated at 37°C, 5% CO<sub>2</sub> for 4 days. On day 5, each well is pulsed with tritiated thymidine (1.0 mCi/well; Amersham). After 6 hours the cells are washed 3 times and then the uptake of the label is evaluated.

35           In another variant of this assay, PBMCs are isolated from the spleens of Balb/c mice and C57B6 mice. The cells are teased from freshly harvested spleens in assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate) and the PBMCs are isolated by overlaying these cells over Lympholyte M (Organon Teknika), centrifuging at 2000

rpm for 20 minutes, collecting and washing the mononuclear cell layer in assay media and resuspending the cells to  $1 \times 10^7$  cells/ml of assay media. The assay is then conducted as described above.

Any decreases below control is considered to be a positive result for an inhibitory compound, with decreases of less than or equal to 80% being preferred. However, any value less than control indicates an inhibitory effect for the test protein.

The following polypeptide tested positive in this assay: PRO1114, PRO836, PRO1159, PRO1312, PRO1192, PRO1195 and PRO1387.

**EXAMPLE 156: Mouse Kidney Mesangial Cell Proliferation Assay (Assay 92)**

This assay shows that certain polypeptides of the invention act to induce proliferation of mammalian kidney mesangial cells and, therefore, are useful for treating kidney disorders associated with decreased mesangial cell function such as Berger disease or other nephropathies associated with Schönlein-Henoch purpura,

celiac disease, dermatitis herpetiformis or Crohn disease. The assay is performed as follows. On day one, mouse kidney mesangial cells are plated on a 96 well plate in growth media (3:1 mixture of Dulbecco's modified Eagle's medium and Ham's F12 medium, 95% fetal bovine serum, 5% supplemented with 14 mM HEPES) and grown overnight. On day 2, PRO polypeptides are diluted at 2 concentrations (1% and 0.1%) in serum-free medium and added to the cells. Control samples are serum-free medium alone. On day 4, 20  $\mu$ l of the Cell Titer 96 Aqueous one solution reagent (Progenia) was added to each well and the colorimetric reaction was allowed to proceed for 2 hours. The absorbance (OD) is then measured at 490 nm. A positive in the assay is anything that gives an absorbance reading which is at least 15% above the control reading.

The following polypeptide tested positive in this assay: PRO819, PRO813 and PRO1066.

**EXAMPLE 157: Pericyte c-Fos Induction (Assay 93)**

This assay shows that certain polypeptides of the invention act to induce the expression of c-fos in pericyte cells and, therefore, are useful not only as diagnostic markers for particular types of pericyte-associated tumors but also for giving rise to antagonists which would be expected to be useful for the therapeutic treatment of pericyte-associated tumors. Specifically, on day 1, pericytes are received from VEC Technologies and all but 5 ml of media is removed from flask. On day 2, the pericytes are trypsinized, washed, spun and then plated onto 96 well plates. On day 7, the media is removed and the pericytes are treated with 100  $\mu$ l of PRO polypeptide test samples and controls (positive control = DME+5% serum +/- PDGF at 500 ng/ml; negative control = protein 32). Replicates are averaged and SD/CV are determined. Fold increase over Protein 32 (buffer control) value indicated by chemiluminescence units (RLU) luminometer reading verses frequency is plotted on a histogram. Two-fold above Protein 32 value is considered positive for the assay. ASY Matrix: Growth media = low glucose DMEM = 20% FBS + 1X pen strep + 1X fungizone. Assay Media = low glucose DMEM +5% FBS.

The following polypeptides tested positive in this assay: PRO943 and PRO819.

EXAMPLE 158: Detection of PRO Polypeptides That Affect Glucose or FFA Uptake by Primary Rat Adipocytes (Assay 94)

This assay is designed to determine whether PRO polypeptides show the ability to affect glucose or FFA uptake by adipocyte cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by adipocytes would be beneficial including, for example, obesity, diabetes or hyper- or hypo-insulinemia.

In a 96 well format, PRO polypeptides to be assayed are added to primary rat adipocytes, and allowed to incubate overnight. Samples are taken at 4 and 16 hours and assayed for glycerol, glucose and FFA uptake. After the 16 hour incubation, insulin is added to the media and allowed to incubate for 4 hours. At this time, a sample is taken and glycerol, glucose and FFA uptake is measured. Media containing insulin without the PRO polypeptide is used as a positive reference control. As the PRO polypeptide being tested may either stimulate or inhibit glucose and FFA uptake, results are scored as positive in the assay if greater than 1.5 times or less than 0.5 times the insulin control.

The following PRO polypeptides tested positive as stimulators of glucose and/or FFA uptake in this assay: PRO1114, PRO1007, PRO1066, PRO848, PRO1182, PRO1198, PRO1192, PRO1271, PRO1375 and PRO1387.

The following PRO polypeptides tested positive as inhibitors of glucose and/or FFA uptake in this assay: PRO1184, PRO1360, PRO1309, PRO1154, PRO1181, PRO1186, PRO1160 and PRO1384.

EXAMPLE 159: Chondrocyte Re-differentiation Assay (Assay 110)

This assay shows that certain polypeptides of the invention act to induce redifferentiation of chondrocytes, therefore, are expected to be useful for the treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis. The assay is performed as follows. Porcine chondrocytes are isolated by overnight collagenase digestion of articular cartilage of metacarpophalangeal joints of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm<sup>2</sup> in Ham F-12 containing 10% FBS and 4 µg/ml gentamycin. The culture media is changed every third day and the cells are then seeded in 96 well plates at 5,000 cells/well in 100 µl of the same media without serum and 100 µl of the test PRO polypeptide, 5 nM staurosporin (positive control) or medium alone (negative control) is added to give a final volume of 200 µl/well. After 5 days of incubation at 37°C, a picture of each well is taken and the differentiation state of the chondrocytes is determined. A positive result in the assay occurs when the redifferentiation of the chondrocytes is determined to be more similar to the positive control than the negative control.

The following polypeptide tested positive in this assay: PRO1282, PRO1310, PRO619, PRO943, PRO820, PRO1080, PRO1016, PRO1007, PRO1056, PRO791, PRO1111, PRO1184, PRO1360, PRO1309, PRO1107, PRO1132, PRO1131, PRO848, PRO1181, PRO1186, PRO1159, PRO1312, PRO1192 and PRO1384.



EXAMPLE 160: Chondrocyte Proliferation Assay (Assay 111)

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to induce the proliferation and/or redifferentiation of chondrocytes in culture. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis.

5 Porcine chondrocytes are isolated by overnight collagenase digestion of articular cartilage of the metacarpophalangeal joint of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm<sup>2</sup> in Ham F-12 containing 10% FBS and 4 µg/ml gentamycin. The culture media is changed every third day and the cells are reseeded to 25,000 cells/cm<sup>2</sup> every five days. On day 12, the cells are seeded in 96 well plates at 5,000 cells/well in 100 µl of the same media without serum and 100 µl of either serum-free medium (negative control), staurosporin (final concentration of 5 nM; positive control) or the test PRO polypeptide are added to give a final volume of 200 µl/well. After 5 days at 37°C, 20 µl of Alamar blue is added to each well and the plates are incubated for an additional 3 hours at 37°C. The fluorescence is then measured in each well (Ex:530 nm; Em: 590 nm). The fluorescence of a plate containing 200 µl of the serum-free medium is measured to obtain the background. A positive result in the assay is obtained when the fluorescence of the PRO polypeptide treated sample is more like that of the positive control than the negative control.

15 The following PRO polypeptides tested positive in this assay: PRO1310, PRO844, PRO1312, PRO1192 and PRO1387.

EXAMPLE 161: Induction of Pancreatic β-Cell Precursor Proliferation (Assay 117)

20 This assay shows that certain polypeptides of the invention act to induce an increase in the number of pancreatic β-cell precursor cells and, therefore, are useful for treating various insulin deficient states in mammals, including diabetes mellitus. The assay is performed as follows. The assay uses a primary culture of mouse fetal pancreatic cells and the primary readout is an alteration in the expression of markers that represent either β-cell precursors or mature β-cells. Marker expression is measured by real time quantitative PCR (RTQ-PCR); wherein the marker being evaluated is a transcription factor called Pdx1.

25 The pancreata are dissected from E14 embryos (CD1 mice). The pancreata are then digested with collagenase/dispase in F12/DMEM at 37°C for 40 to 60 minutes (collagenase/dispase, 1.37 mg/ml, Boehringer Mannheim, #1097113). The digestion is then neutralized with an equal volume of 5% BSA and the cells are washed once with RPMI1640. At day 1, the cells are seeded into 12-well tissue culture plates (pre-coated with laminin, 20 µg/ml in PBS, Boehringer Mannheim, #124317). Cells from pancreata from 1-2 embryos are distributed per well. The culture medium for this primary culture is 14F/1640. At day 2, the media is removed and the attached cells washed with RPMI/1640. Two mls of minimal media are added in addition to the protein to be tested. At day 4, the media is removed and RNA prepared from the cells and marker expression analyzed by real time quantitative RT-PCR. A protein is considered to be active in the assay if it increases the expression of the relevant β-cell marker as compared to untreated controls.

35 14F/1640 is RPMI1640 (Gibco) plus the following:

group A 1:1000

group B 1:1000

recombinant human insulin 10  $\mu\text{g/ml}$

Aprotinin (50 $\mu\text{g/ml}$ ) 1:2000 (Boehringer manheim #981532)

Bovine pituitary extract (BPE) 60 $\mu\text{g/ml}$

Gentamycin 100 ng/ml

Group A : (in 10ml PBS)

Transferrin, 100mg (Sigma T2252)

Epidermal Growth Factor, 100 $\mu\text{g}$  (BRL 100004)

Triiodothyronine, 10 $\mu\text{l}$  of  $5 \times 10^{-6}$  M (Sigma T5516)

Ethanolamine, 100 $\mu\text{l}$  of  $10^{-1}$  M (Sigma E0135)

Phosphoethalamine, 100 $\mu\text{l}$  of  $10^{-1}$  M (Sigma P0503)

Selenium, 4 $\mu\text{l}$  of  $10^{-1}$  M (Aesar #12574)

Group C : (in 10ml 100% ethanol)

Hydrocortisone, 2 $\mu\text{l}$  of  $5 \times 10^{-3}$  M (Sigma #H0135)

Progesterone, 100 $\mu\text{l}$  of  $1 \times 10^{-3}$  M (Sigma #P6149)

Forskolin, 500 $\mu\text{l}$  of 20mM (Calbiochem #344270)

Minimal media:

RPMI 1640 plus transferrin (10  $\mu\text{g/ml}$ ), insulin (1  $\mu\text{g/ml}$ ), gentamycin (100 ng/ml), aprotinin (50  $\mu\text{g/ml}$ ) and BPE (15  $\mu\text{g/ml}$ ).

Defined media:

RPMI 1640 plus transferrin (10  $\mu\text{g/ml}$ ), insulin (1  $\mu\text{g/ml}$ ), gentamycin (100 ng/ml) and aprotinin (50  $\mu\text{g/ml}$ ).

The following polypeptides tested positive in this assay: PRO1310, PRO1188, PRO1131 and PRO1387.

#### EXAMPLE 162: Detection of Polypeptides That Affect Glucose or FFA Uptake in Skeletal Muscle (Assay 106)

This assay is designed to determine whether PRO polypeptides show the ability to affect glucose or FFA uptake by skeletal muscle cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by skeletal muscle would be beneficial including, for example, diabetes or hyper- or hypo-insulinemia.

In a 96 well format, PRO polypeptides to be assayed are added to primary rat differentiated skeletal muscle, and allowed to incubate overnight. Then fresh media with the PRO polypeptide and +/- insulin are added to the wells. The sample media is then monitored to determine glucose and FFA uptake by the skeletal muscle cells. The insulin will stimulate glucose and FFA uptake by the skeletal muscle, and insulin in media without the PRO polypeptide is used as a positive control, and a limit for scoring. As the PRO polypeptide being tested may either stimulate or inhibit glucose and FFA uptake, results are scored as positive in the assay

if greater than 1.5 times or less than 0.5 times the insulin control.

The following PRO polypeptides tested positive as either stimulators or inhibitors of glucose and/or FFA uptake in this assay: PRO358, PRO1016, PRO1007, PRO826, PRO1066, PRO1029 and PRO1309.

EXAMPLE 163: Fetal Hemoglobin Induction in an Erythroblastic Cell Line (Assay 107)

This assay is useful for screening PRO polypeptides for the ability to induce the switch from adult hemoglobin to fetal hemoglobin in an erythroblastic cell line. Molecules testing positive in this assay are expected to be useful for therapeutically treating various mammalian hemoglobin-associated disorders such as the various thalassemias. The assay is performed as follows. Erythroblastic cells are plated in standard growth medium at 1000 cells/well in a 96 well format. PRO polypeptides are added to the growth medium at a concentration of 0.2% or 2% and the cells are incubated for 5 days at 37°C. As a positive control, cells are treated with 100 $\mu$ M hemin and as a negative control, the cells are untreated. After 5 days, cell lysates are prepared and analyzed for the expression of gamma globin (a fetal marker). A positive in the assay is a gamma globin level at least 2-fold above the negative control.

The following polypeptides tested positive in this assay: PRO1114, PRO826, PRO1066, PRO844, PRO1192 and PRO1358.

EXAMPLE 164: Induction of Pancreatic  $\beta$ -Cell Precursor Differentiation (Assay 89)

This assay shows that certain polypeptides of the invention act to induce differentiation of pancreatic  $\beta$ -cell precursor cells into mature pancreatic  $\beta$ -cells and, therefore, are useful for treating various insulin deficient states in mammals, including diabetes mellitus. The assay is performed as follows. The assay uses a primary culture of mouse fetal pancreatic cells and the primary readout is an alteration in the expression of markers that represent either  $\beta$ -cell precursors or mature  $\beta$ -cells. Marker expression is measured by real time quantitative PCR (RTQ-PCR); wherein the marker being evaluated is insulin.

The pancreata are dissected from E14 embryos (CD1 mice). The pancreata are then digested with collagenase/dispase in F12/DMEM at 37°C for 40 to 60 minutes (collagenase/dispase, 1.37 mg/ml, Boehringer Mannheim, #1097113). The digestion is then neutralized with an equal volume of 5% BSA and the cells are washed once with RPMI1640. At day 1, the cells are seeded into 12-well tissue culture plates (pre-coated with laminin, 20 $\mu$ g/ml in PBS, Boehringer Mannheim, #124317). Cells from pancreata from 1-2 embryos are distributed per well. The culture medium for this primary culture is 14F/1640. At day 2, the media is removed and the attached cells washed with RPMI/1640. Two mls of minimal media are added in addition to the protein to be tested. At day 4, the media is removed and RNA prepared from the cells and marker expression analyzed by real time quantitative RT-PCR. A protein is considered to be active in the assay if it increases the expression of the relevant  $\beta$ -cell marker as compared to untreated controls.

14F/1640 is RPMI1640 (Gibco) plus the following:

group A 1:1000

group B 1:1000

recombinant human insulin 10  $\mu$ g/ml

Aprotinin (50 $\mu$ g/ml) 1:2000 (Boehringer manheim #981532)

Bovine pituitary extract (BPE) 60 $\mu$ g/ml

Gentamycin 100 ng/ml

Group A : (in 10ml PBS)

Transferrin, 100mg (Sigma T2252)

5 Epidermal Growth Factor, 100 $\mu$ g (BRL 100004)

Triiodothyronine, 10 $\mu$ l of 5x10<sup>-6</sup> M (Sigma T5516)

Ethanolamine, 100 $\mu$ l of 10<sup>-1</sup> M (Sigma E0135)

Phosphoethalamine, 100 $\mu$ l of 10<sup>-1</sup> M (Sigma P0503)

Selenium, 4 $\mu$ l of 10<sup>-1</sup> M (Aesar #12574)

10 Group C : (in 10ml 100% ethanol)

Hydrocortisone, 2 $\mu$ l of 5X10<sup>-3</sup> M (Sigma #H0135)

Progesterone, 100 $\mu$ l of 1X10<sup>-3</sup> M (Sigma #P6149)

Forskolin, 500 $\mu$ l of 20mM (Calbiochem #344270)

Minimal media:

15 RPMI 1640 plus transferrin (10  $\mu$ g/ml), insulin (1  $\mu$ g/ml), gentamycin (100 ng/ml), aprotinin (50  $\mu$ g/ml) and BPE (15  $\mu$ g/ml).

Defined media:

RPMI 1640 plus transferrin (10  $\mu$ g/ml), insulin (1  $\mu$ g/ml), gentamycin (100 ng/ml) and aprotinin (50  $\mu$ g/ml).

20 The following polypeptides were positive in this assay: PRO1188, PRO1132, PRO1131 and PRO1181.

#### EXAMPLE 165: Skin Vascular Permeability Assay (Assay 64)

25 This assay shows that certain polypeptides of the invention stimulate an immune response and induce inflammation by inducing mononuclear cell, eosinophil and PMN infiltration at the site of injection of the animal. Compounds which stimulate an immune response are useful therapeutically where stimulation of an immune response is beneficial. This skin vascular permeability assay is conducted as follows. Hairless guinea pigs weighing 350 grams or more are anesthetized with ketamine (75-80 mg/Kg) and 5 mg/Kg xylazine intramuscularly (IM). A sample of purified polypeptide of the invention or a conditioned media test sample

30 is injected intradermally onto the backs of the test animals with 100  $\mu$ l per injection site. It is possible to have about 10-30, preferably about 16-24, injection sites per animal. One  $\mu$ l of Evans blue dye (1% in physiologic buffered saline) is injected intracardially. Blemishes at the injection sites are then measured (mm diameter) at 1 hr and 6 hr post injection. Animals were sacrificed at 6 hrs after injection. Each skin injection site is biopsied and fixed in formalin. The skins are then prepared for histopathologic evaluation. Each site is

35 evaluated for inflammatory cell infiltration into the skin. Sites with visible inflammatory cell inflammation are scored as positive. Inflammatory cells may be neutrophilic, eosinophilic, monocytic or lymphocytic. At least a minimal perivascular infiltrate at the injection site is scored as positive, no infiltrate at the site of injection is

scored as negative.

The following polypeptide tested positive in this assay: PRO1007, PRO1358 and PRO1375.

EXAMPLE 166: Induction of Endothelial Cell Apoptosis (ELISA) (Assay 109)

The ability of PRO polypeptides to induce apoptosis in endothelial cells was tested in human venous umbilical vein endothelial cells (HUVEC, Cell Systems) using a 96-well format, in 0% serum media supplemented with 100 ng/ml VEGF, 0.1 % BSA, 1X penn/strep. A positive result in this assay indicates the usefulness of the polypeptide for therapeutically treating any of a variety of conditions associated with undesired endothelial cell growth including, for example, the inhibition of tumor growth. The 96-well plates used were manufactured by Falcon (No. 3072). Coating of 96 well plates were prepared by allowing gelatinization to occur for >30 minutes with 100  $\mu$ l of 0.2% gelatin in PBS solution. The gelatin mix was aspirated thoroughly before plating HUVEC cells at a final concentration of  $2 \times 10^4$  cells/ml in 10% serum containing medium - 100  $\mu$ l volume per well. The cells were grown for 24 hours before adding test samples containing the PRO polypeptide of interest.

To all wells, 100  $\mu$ l of 0% serum media (Cell Systems) complemented with 100 ng/ml VEGF, 0.1 % BSA, 1X penn/strep was added. Test samples containing PRO polypeptides were added in triplicate at dilutions of 1%, 0.33% and 0.11%. Wells without cells were used as a blank and wells with cells only were used as a negative control. As a positive control, 1:3 serial dilutions of 50  $\mu$ l of a 3x stock of staurosporine were used. The cells were incubated for 24 to 35 hours prior to ELISA.

ELISA was used to determine levels of apoptosis preparing solutions according to the Boehringer Manual [Boehringer, Cell Death Detection ELISA plus, Cat No. 1 920 685]. Sample preparations: 96 well plates were spun down at 1 krpm for 10 minutes (200g); the supernatant was removed by fast inversion, placing the plate upside down on a paper towel to remove residual liquid. To each well, 200  $\mu$ l of 1X Lysis buffer was added and incubation allowed at room temperature for 30 minutes without shaking. The plates were spun down for 10 minutes at 1 krpm, and 20  $\mu$ l of the lysate (cytoplasmic fraction) was transferred into streptavidin coated MTP. 80  $\mu$ l of immunoreagent mix was added to the 20  $\mu$ l lysate in each well. The MTP was covered with adhesive foil and incubated at room temperature for 2 hours by placing it on an orbital shaker (200 rpm). After two hours, the supernatant was removed by suction and the wells rinsed three times with 250  $\mu$ l of 1X incubation buffer per well (removed by suction). Substrate solution was added (100  $\mu$ l) into each well and incubated on an orbital shaker at room temperature at 250 rpm until color development was sufficient for a photometric analysis (approx. after 10-20 minutes). A 96 well reader was used to read the plates at 405 nm, reference wavelength, 492 nm. The levels obtained for PIN 32 (control buffer) was set to 100%. Samples with levels > 130% were considered positive for induction of apoptosis.

The following PRO polypeptides tested positive in this assay: PRO844.

EXAMPLE 167: Guinea Pig Vascular Leak (Assay 32)

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to induce vascular permeability. Polypeptides testing positive in this assay are expected to be useful

for the therapeutic treatment of conditions which would benefit from enhanced vascular permeability including, for example, conditions which may benefit from enhanced local immune system cell infiltration.

Hairless guinea pigs weighing 350 grams or more were anesthetized with Ketamine (75-80 mg/kg) and 5 mg/kg Xylazine intramuscularly. Test samples containing the PRO polypeptide or a physiological buffer without the test polypeptide are injected into skin on the back of the test animals with 100  $\mu$ l per injection site intradermally. There were approximately 16-24 injection sites per animal. One ml of Evans blue dye (1% in PBS) is then injected intracardially. Skin vascular permeability responses to the compounds (*i.e.*, blemishes at the injection sites of injection) are visually scored by measuring the diameter (in mm) of blue-colored leaks from the site of injection at 1, 6 and 24 hours post administration of the test materials. The mm diameter of blueness at the site of injection is observed and recorded as well as the severity of the vascular leakage. Blemishes of at least 5 mm in diameter are considered positive for the assay when testing purified proteins, being indicative of the ability to induce vascular leakage or permeability. A response greater than 7 mm diameter is considered positive for conditioned media samples. Human VEGF at 0.1  $\mu$ g/100  $\mu$ l is used as a positive control, inducing a response of 4-8 mm diameter.

The following PRO polypeptides tested positive in this assay: PRO1155.

**EXAMPLE 168: Mouse Mesengial Cell Inhibition Assay (Assay 114)**

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to inhibit the proliferation of mouse mesengial cells in culture. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of such diseases or conditions where inhibition of mesengial cell proliferation would be beneficial such as, for example, cystic renal dysplasia, polycystic kidney disease, or other kidney disease associated with abnormal mesengial cell proliferation, renal tumors, and the like.

On day 1, mouse mesengial cells are plated on a 96 well plate in growth medium (a 3:1 mixture of Dulbecco's modified Eagle's medium and Ham's F12 medium, 95%; fetal bovine serum, 5%; supplemented with 14mM HEPES) and then are allowed to grow overnight. On day 2, the PRO polypeptide is diluted at 2 different concentrations (1%, 0.1%) in serum-free medium and is added to the cells. The negative control is growth medium without added PRO polypeptide. After the cells are allowed to incubate for 48 hours, 20  $\mu$ l of the Cell Titer 96 Aqueous one solution reagent (Promega) is added to each well and the colormetric reaction is allowed to proceed for 2 hours. The absorbance (OD) is then measured at 490 nm. A positive in the assay is an absorbance reading which is at least 10% above the negative control.

The following PRO polypeptides tested positive in this assay: PRO1192 and PRO1195.

**Example 169: *In Vitro* Antitumor Assay (Assay 161)**

The antiproliferative activity of various PRO polypeptides was determined in the investigational, disease-oriented *in vitro* anti-cancer drug discovery assay of the National Cancer Institute (NCI), using a sulforhodamine B (SRB) dye binding assay essentially as described by Skehan et al., J. Natl. Cancer Inst. 82:1107-1112 (1990). The 60 tumor cell lines employed in this study ("the NCI panel"), as well as conditions

for their maintenance and culture *in vitro* have been described by Monks et al., J. Natl. Cancer Inst. 83:757-766 (1991). The purpose of this screen is to initially evaluate the cytotoxic and/or cytostatic activity of the test compounds against different types of tumors (Monks et al., *supra*; Boyd, Cancer: Princ. Pract. Oncol. Update 3(10):1-12 [1989]).

Cells from approximately 60 human tumor cell lines were harvested with trypsin/EDTA (Gibco), washed once, resuspended in IMEM and their viability was determined. The cell suspensions were added by pipet (100  $\mu$ L volume) into separate 96-well microtiter plates. The cell density for the 6-day incubation was less than for the 2-day incubation to prevent overgrowth. Inoculates were allowed a preincubation period of 24 hours at 37°C for stabilization. Dilutions at twice the intended test concentration were added at time zero in 100  $\mu$ L aliquots to the microtiter plate wells (1:2 dilution). Test compounds were evaluated at five half-log dilutions (1000 to 100,000-fold). Incubations took place for two days and six days in a 5% CO<sub>2</sub> atmosphere and 100% humidity.

After incubation, the medium was removed and the cells were fixed in 0.1 ml of 10% trichloroacetic acid at 40°C. The plates were rinsed five times with deionized water, dried, stained for 30 minutes with 0.1 ml of 0.4% sulforhodamine B dye (Sigma) dissolved in 1% acetic acid, rinsed four times with 1% acetic acid to remove unbound dye, dried, and the stain was extracted for five minutes with 0.1 ml of 10 mM Tris base [tris(hydroxymethyl)aminomethane], pH 10.5. The absorbance (OD) of sulforhodamine B at 492 nm was measured using a computer-interfaced, 96-well microtiter plate reader.

A test sample is considered positive if it shows at least 50% growth inhibitory effect at one or more concentrations. The results are shown in the following table, where the abbreviations are as follows:

NSCL = non-small cell lung carcinoma

CNS = central nervous system

Table 7

<u>Test compound</u>	<u>Concentration</u>	<u>Days</u>	<u>Tumor Cell Line Type</u>	<u>C e l l L i n e Designation</u>
PRO1016	0.1 nM	2	Leukemia	K-568
PRO1016	0.1 nM	2	Leukemia	MOLT-4
PRO1016	0.1 nM	2	Leukemia	RPMI-8226
PRO1016	0.1 nM	2	NSCL	A549/ATCC
PRO1016	0.1 nM	2	NSCL	EKVX
PRO1016	0.1 nM	2	NSCL	NCI-H23
PRO1016	0.1 nM	2	NSCL	NCI-H522
PRO1016	0.1 nM	2	Colon	KM-12
PRO1016	0.1 nM	2	CNS	SF-295
PRO1016	0.1 nM	2	Melanoma	SK-MEL-5
PRO1016	0.1 nM	2	Melanoma	UACC-257
PRO1016	0.1 nM	2	Ovarian	OVCAR-3
PRO1016	0.1 nM	2	Ovarian	OVCAR-4
PRO1016	0.1 nM	2	Breast	NCI/SDR-RES
PRO1016	0.1 nM	2	Breast	T-47D
PRO1016	0.1 nM	6	Leukemia	CCRF-CEM
PRO1016	0.1 nM	6	Leukemia	K-562

Table 7 (cont')

	<u>Test compound</u>	<u>Concentration</u>	<u>Days</u>	<u>Tumor Cell Line Type</u>	<u>C e l l L i n e Designation</u>
5	PRO1016	0.1 nM	6	Leukemia	MOLT-4
	PRO1016	0.1 nM	6	Leukemia	RPMI-8226
	PRO1016	0.1 nM	6	NSCL	A549/ATCC
	PRO1016	0.1 nM	6	NSCL	EKVX
	PRO1016	0.1 nM	6	NSCL	HOP-62
10	PRO1016	0.1 nM	6	NSCL	NCI-H23
	PRO1016	0.1 nM	6	NSCL	NCI-H322M
	PRO1016	0.1 nM	6	NSCL	NCI-H460
	PRO1016	0.1 nM	6	NSCL	NCI-H522
	PRO1016	0.1 nM	6	Colon	COLO 205
15	PRO1016	0.1 nM	6	Colon	CHT-116
	PRO1016	0.1 nM	6	Colon	HCT-15
	PRO1016	0.1 nM	6	Colon	HT-29
	PRO1016	0.1 nM	6	Colon	SW-620
	PRO1016	0.1 nM	6	CNS	SF-295
20	PRO1016	0.1 nM	6	CNS	SF-539
	PRO1016	0.1 nM	6	CNS	SNB-19
	PRO1016	0.1 nM	6	CNS	U251
	PRO1016	0.1 nM	6	Melanoma	LOX IMVI
	PRO1016	0.1 nM	6	Melanoma	MALME-3M
25	PRO1016	0.1 nM	6	Melanoma	SK-MEL-28
	PRO1016	0.1 nM	6	Melanoma	SK-MEL-5
	PRO1016	0.1 nM	6	Melanoma	UACC-257
	PRO1016	0.1 nM	6	Melanoma	UACC-62
	PRO1016	0.1 nM	6	Ovarian	IGROV1
30	PRO1016	0.1 nM	6	Ovarian	OVCAR-3
	PRO1016	0.1 nM	6	Ovarian	OVCAR-4
	PRO1016	0.1 nM	6	Ovarian	OVCAR-8
	PRO1016	0.1 nM	6	Renal	ACHN
	PRO1016	0.1 nM	6	Renal	RXF 393
35	PRO1016	0.1 nM	6	Renal	SN12C
	PRO1016	0.1 nM	6	Renal	TK-10
	PRO1016	0.1 nM	6	Prostate	PC-3
	PRO1016	0.1 nM	6	Breast	MCF-7
	PRO1016	0.1 nM	6	Breast	NCI/ADR-RES
40	PRO1016	0.1 nM	6	Breast	MDA-MB-231
	PRO1016	0.1 nM	6	Breast	MDA-MB-435
	PRO1016	0.1 nM	6	Breast	MDA-N
	PRO1016	0.1 nM	6	Breast	BT-549
	PRO1016	0.1 nM	6	Breast	T-47D
45	PRO1186	95 nM	2	NSCL	NCI-H226
	PRO1186	95 nM	2	Colon	Colo205
	PRO1186	2.2 nM	6	Breast	MDA-N
	PRO1186	114 nM	2	NSCL	NCI-H322M
	PRO1186	114 nM	2	CNS	SF-268; SF-539
50	PRO1186	114 nM	2	Ovarian	IGFOV1
	PRO1186	114 nM	2	Renal	786-0; SN12C; TK-10
	PRO1186	114 nM	6	Leukemia	MOLT-4; RPMI-8226
	PRO1186	114 nM	6	Melanoma	LOX IMVI
	PRO1186	114 nM	6	Ovarian	OVCAR-4; SK-OV-3



Table 7 (cont')

	<u>Test compound</u>	<u>Concentration</u>	<u>Days</u>	<u>Tumor Cell Line Type</u>	<u>C e l l L i n e Designation</u>
	PRO1186	114 nM	6	Breast	MDA-MB-435; T-47D
5	PRO1186	8.1 nM	6	Leukemia	K-562
	PRO1186	8.1 nM	6	NSCL	HOP-62
	PRO1186	8.1 nM	6	Colon	Colo205; HCC-2998
	PRO1186	8.1 nM	6	Breast	T-47D
	PRO1186	15.4 nM	6	Leukemia	K-562
10	PRO1186	3.6 nM	2	Ovarian	OVCAR-3
	PRO1186	3.6 nM	6	NSCL	HOP-62

The results of these assays demonstrate that the positive testing PRO polypeptides are useful for inhibiting neoplastic growth in a number of different tumor cell types and may be used therapeutically therefor.. Antibodies against these PRO polypeptides are useful for affinity purification of these useful polypeptides. Nucleic acids encoding these PRO polypeptides are useful for the recombinant preparation of these polypeptides.

#### EXAMPLE 170: Gene Amplification in Tumors

This example shows that certain PRO polypeptide-encoding genes are amplified in the genome of certain human lung, colon and/or breast cancers and/or cell lines. Amplification is associated with overexpression of the gene product, indicating that the polypeptides are useful targets for therapeutic intervention in certain cancers such as colon, lung, breast and other cancers and diagnostic determination of the presence of those cancers. Therapeutic agents may take the form of antagonists of the PRO polypeptide, for example, murine-human chimeric, humanized or human antibodies against a PRO polypeptide.

The starting material for the screen was genomic DNA isolated from a variety cancers. The DNA is quantitated precisely, *e.g.*, fluorometrically. As a negative control, DNA was isolated from the cells of ten normal healthy individuals which was pooled and used as assay controls for the gene copy in healthy individuals (not shown). The 5' nuclease assay (for example, TaqMan™) and real-time quantitative PCR (for example, ABI Prizm 7700 Sequence Detection System™ (Perkin Elmer, Applied Biosystems Division, Foster City, CA)), were used to find genes potentially amplified in certain cancers. The results were used to determine whether the DNA encoding the PRO polypeptide is over-represented in any of the primary lung or colon cancers or cancer cell lines or breast cancer cell lines that were screened. The primary lung cancers were obtained from individuals with tumors of the type and stage as indicated in Table 8. An explanation of the abbreviations used for the designation of the primary tumors listed in Table 8 and the primary tumors and cell lines referred to throughout this example are given below.

The results of the TaqMan™ are reported in delta ( $\Delta$ ) Ct units. One unit corresponds to 1 PCR cycle or approximately a 2-fold amplification relative to normal, two units corresponds to 4-fold, 3 units to 8-fold amplification and so on. Quantitation was obtained using primers and a TaqMan™ fluorescent probe derived from the PRO polypeptide-encoding gene. Regions of the PRO polypeptide-encoding gene which are most likely to contain unique nucleic acid sequences and which are least likely to have spliced out introns are

preferred for the primer and probe derivation, *e.g.*, 3'-untranslated regions. The sequences for the primers and probes (forward, reverse and probe) used for the PRO polypeptide gene amplification analysis were as follows:

PRO290 (DNA35680-1212):

35680.tm.p:

5 5'-CCACCAATGGCAGCCCCACCT-3' (SEQ ID NO:428)

35680.tm.f:

5'-GACTGCCCTCCCTGCCA-3' (SEQ ID NO:429)

35680.tm.r:

10 5'-CAAAAAGCCTGGAAGTCTTCAAAG-3' (SEQ ID NO:430)

PRO341 (DNA26288-1239):

26288.tm.fl:

5'-CAGCTGGACTGCAGGTGCTA-3' (SEQ ID NO:431)

26288.tm.rl:

15 5'-CAGTGAGCACAGCAAGTGTCCCT-3' (SEQ ID NO:432)

26288.tm.pl:

5'-GGCCACCTCCTTGAGTCTTCAGTTCCT-3' (SEQ ID NO:433)

PRO535 (DNA49143-1429):

20 49143.tm.fl:

5'-CAACTACTGGCTAAAGCTGGTGAA-3' (SEQ ID NO:434)

49143.tm.rl:

5'-CCTTTCTGTATAGGTGATACCCAATGA-3' (SEQ ID NO:435)

49143.tm.pl:

25 5'-TGGCCATCCCTACCAGAGGCAAAA-3' (SEQ ID NO:436)

PRO619 (DNA49821-1562):

49821.tm.fl:

5'-CTGAAGACGACGCGGATTACTA-3' (SEQ ID NO:437)

30 49821.tm.rl:

5'-GGCAGAAATGGGAGGCAGA-3' (SEQ ID NO:438)

49821.tm.pl:

5'-TGCTCTGTTGGCTACGGCTTTAGTCCCTAG-3' (SEQ ID NO:439)

35 PRO809 (DNA57836-1338):

57836.tm.fl:

5'-AGCAGCAGCCATGTAGAATGAA-3' (SEQ ID NO:440)

57836.tm.r1:

5'-AATACGAACAGTGCACGCTGAT-3' (SEQ ID NO:441)

57836.tm.p1:

5'-TCCAGAGAGCCAAGCACGGCAGA-3' (SEQ ID NO:442)

5 PRO830 (DNA56866-1342):56866.tm.fl:

5'-TCTAGCCAGCTTGGCTCCAATA-3' (SEQ ID NO:443)

56866.tm.r1:

5'-CCTGGCTCTAGCACCAACTCATA-3' (SEQ ID NO:444)

10 56866.tm.p1:

5'-TCAGTGGCCCTAAGGAGATGGGCCT-3' (SEQ ID NO:445)

PRO848 (DNA59839-1461):59839.tm.fl:

15 5'-CAGGATACAGTGGGAATCTTGAGA-3' (SEQ ID NO:446)

59839.tm.r1:

5'-CCTGAAGGGCTTGGAGCTTAGT-3' (SEQ ID NO:447)

59839.tm.p1:

5'-TCTTTGGCCATTTCCCATGGCTCA-3' (SEQ ID NO:448)

20

PRO943 (DNA52192-1369):52192.tm.fl:

5'-CCCATGGCGAGGAGGAAT-3' (SEQ ID NO:449)

52192.tm.r1:

25 5'-TGC GTACGTGTGCCTTCAG-3' (SEQ ID NO:450)

52192.tm.p1:

5'-CAGCACCCCAGGCAGTCTGTGTGT-3' (SEQ ID NO:451)

PRO1005 (DNA57708-1411):30 57708.tm.fl:

5'-AACGTGCTACACGACCAGTGTACT-3' (SEQ ID NO:452)

57708.tm.r1:

5'-CACAGCATATTCAGATGACTAAATCCA-3' (SEQ ID NO:453)

57708.tm.p1:

35 5'-TTGTTTAGTTCTCCACCGTGTCTCCACAGAA-3' (SEQ ID NO:454)

PRO1009 (DNA57129-1413):57129.tm.fl:

5'-TGTCAGAATGCAACCTGGCTT-3' (SEQ ID NO:455)

57129.tm.r1:

5'-TGATGTGCCTGGCTCAGAAC-3' (SEQ ID NO:456)

5 57129.tm.p1:

5'-TGCACCTAGATGTCCCCAGCACCC-3' (SEQ ID NO:457)

PRO1097 (DNA59841-1460):59841.tm.fl:

10 5'-AAGATGCGCCAGGCTTCTTA-3' (SEQ ID NO:458)

59841.tm.r1:

5'-CTCCTGTACGGTCTGCTCACTTAT-3' (SEQ ID NO:459)

59841.tm.p1:

15 5'-TGGCTGTCAGTCCAGTGTGCATGG-3' (SEQ ID NO:460)

PRO1107 (DNA59606-1471):59606.tm.fl:

5'-GCATAGGGATAGATAAGATCCTGCTTTAT-3' (SEQ ID NO:461)

59606.tm.r1:

20 5'-CAAATTAAAGTACCCATCAGGAGAGAA-3' (SEQ ID NO:462)

59606.tm.p1:

5'-AAGTTGCTAAATATATACATTATCTGCGCCAAGTCCA-3' (SEQ ID NO:463)

PRO1111 (DNA58721-1475):25 58721.tm.fl:

5'-GTGCTGCCCACAATTCATGA-3' (SEQ ID NO:464)

58721.tm.r1:

5'-GTCCTTGGTATGGGTCTGAATTATAT-3' (SEQ ID NO:465)

58721.tm.p1:

30 5'-ACTCTCTGCACCCACAGTCACCACTATCTC-3' (SEQ ID NO:466)

PRO1153 (DNA59842-1502):59842.tm.fl:

5'-CTGAGGAACCAGCCATGTCTCT-3' (SEQ ID NO:467)

35 59842.tm.r1:

5'-GACCAGATGCAGGTACAGGATGA-3' (SEQ ID NO:468)

59842.tm.pl:

5'-CTGCCCCTTCAGTGATGCCAACCTT-3' (SEQ ID NO:469)

PRO1182 (DNA59848-1512):59848.tm.fl:

5 5'-GGGTGGAGGCTCACTGAGTAGA-3' (SEQ ID NO:470)

59848.tm.rl:

5'-CAATACAGGTAATGAAACTCTGCTTCTT-3' (SEQ ID NO:471)

59848.tm.pl:

10 5'-TCCTCTTAAGCATAGGCCATTTTCTCAGTTTAGACA-3' (SEQ ID NO:472)

PRO1184 (DNA59220-1514):59220.tm.fl:

5'-GGTGGTCTTGCTTGGTCTCAC-3' (SEQ ID NO:473)

59220.tm.rl:

15 5'-CCGTCGTTTCAGCAACATGAC-3' (SEQ ID NO:474)

59220.tm.pl:

5'-ACCGCCTACCGCTGTGCCCA-3' (SEQ ID NO:475)

PRO1187 (DNA62876-1517):

20 62876.tm.fl:

5'-CAGTAAAACACAGGCTGGATTT-3' (SEQ ID NO:476)

62876.tm.rl:

5'-CCTGAGAGCAAGAAGGTTGAGAAT-3' (SEQ ID NO:477)

62876.tm.pl:

25 5'-TAGACAGGGACCATGGCCCGCA-3' (SEQ ID NO:478)

PRO1281 (DNA59820-1549):59820.tm.fl:

5'-TGGGCTGTAGAAGAGTTGTTG-3' (SEQ ID NO:479)

30 59820.tm.rl:

5'-TCCACACTTGGCCAGTTTAT-3' (SEQ ID NO:480)

59820.tm.pl:

5'-CCCAACTTCTCCCTTTTGGACCCT-3' (SEQ ID NO:481)

35 PRO1112 (DNA57702-1476):

57702.tm.fl

5'-GTCCCTTCACTGTTTAGAGCATGA-3' (SEQ ID NO:482)

57702.tm.p1

5'-ACTCTCCCCCTCAACAGCCTCCTGAG-3' (SEQ ID NO:483)

57702.tm.r1

5'-GTGGTCAGGGCAGATCCTTT-3' (SEQ ID NO:484)

5 PRO1185 (DNA62881-1515):62881.tm.fl:

5'-ACAGATCCAGGAGAGACTCCACA -3' (SEQ ID NO:485)

62881.tm.p1:

5'-AGCGGCGCTCCCAGCCTGAAT -3' (SEQ ID NO:486)

10 62881.tm.r1:

5'-CATGATTGGTCCTCAGTTCCATC -3' (SEQ ID NO:487)

PRO1245 (DNA64884-1527):64884.tm.fl:

15 5'-ATAGAGGGCTCCCAGAAGTG -3' (SEQ ID NO:488)

64884.tm.p1:

5'-CAGGGCCTTCAGGGCCTTCAC-3' (SEQ ID NO:489)

64884.tm.r1:

5'-GCTCAGCCAAACACTGTCA-3' (SEQ ID NO:490)

20 64884.tm.f2:

5'-GGGGCCCTGACAGTGTT -3' (SEQ ID NO:491)

64884.tm.p2:

5'-CTGAGCCGAGACTGGAGCATCTACAC-3' (SEQ ID NO:492)

64884.tm.r2:

25 5'-GTGGGCAGCGTCTTGTC-3' (SEQ ID NO:493)

The 5' nuclease assay reaction is a fluorescent PCR-based technique which makes use of the 5' exonuclease activity of Taq DNA polymerase enzyme to monitor amplification in real time. Two oligonucleotide primers (forward [.f] and reverse [.r]) are used to generate an amplicon typical of a PCR reaction. A third oligonucleotide, or probe (.p), is designed to detect nucleotide sequence located between the two PCR primers. The probe is non-extendible by Taq DNA polymerase enzyme, and is labeled with a reporter fluorescent dye and a quencher fluorescent dye. Any laser-induced emission from the reporter dye is quenched by the quenching dye when the two dyes are located close together as they are on the probe. During the amplification reaction, the Taq DNA polymerase enzyme cleaves the probe in a template-dependent manner. The resultant probe fragments disassociate in solution, and signal from the released reporter dye is free from the quenching effect of the second fluorophore. One molecule of reporter dye is liberated for each new molecule synthesized, and detection of the unquenched reporter dye provides the basis for quantitative interpretation of the data.

The 5' nuclease procedure is run on a real-time quantitative PCR device such as the ABI Prism 7700TM Sequence Detection. The system consists of a thermocycler, laser, charge-coupled device (CCD) camera and computer. The system amplifies samples in a 96-well format on a thermocycler. During amplification, laser-induced fluorescent signal is collected in real-time through fiber optics cables for all 96 wells, and detected at the CCD. The system includes software for running the instrument and for analyzing the data.

5' Nuclease assay data are initially expressed as Ct, or the threshold cycle. This is defined as the cycle at which the reporter signal accumulates above the background level of fluorescence. The  $\Delta C_t$  values are used as quantitative measurement of the relative number of starting copies of a particular target sequence in a nucleic acid sample when comparing cancer DNA results to normal human DNA results.

Table 8 describes the stage, T stage and N stage of various primary tumors which were used to screen the PRO polypeptide compounds of the invention.

Table 8  
Primary Lung and Colon Tumor Profiles

	<u>Primary Tumor Stage</u>	<u>Stage</u>	<u>Other Stage</u>	<u>Dukes Stage</u>	<u>T Stage</u>	<u>N Stage</u>
5	Human lung tumor AdenoCa (SRCC724) [LT1]	IIA			T1	N1
	Human lung tumor SqCCa (SRCC725) [LT1a]	IIB			T3	N0
	Human lung tumor AdenoCa (SRCC726) [LT2]	IB			T2	N0
	Human lung tumor AdenoCa (SRCC727) [LT3]	IIIA			T1	N2
	Human lung tumor AdenoCa (SRCC728) [LT4]	IB			T2	N0
	Human lung tumor SqCCa (SRCC729) [LT6]	IB			T2	N0
10	Human lung tumor Aden/SqCCa (SRCC730) [LT7]	IA			T1	N0
	Human lung tumor AdenoCa (SRCC731) [LT9]	IB			T2	N0
	Human lung tumor SqCCa (SRCC732) [LT10]	IIB			T2	N1
	Human lung tumor SqCCa (SRCC733) [LT11]	IIA			T1	N1
	Human lung tumor AdenoCa (SRCC734) [LT12]	IV			T2	N0
15	Human lung tumor AdenoSqCCa (SRCC735)[LT13]	IB			T2	N0
	Human lung tumor SqCCa (SRCC736) [LT15]	IB			T2	N0
	Human lung tumor SqCCa (SRCC737) [LT16]	IB			T2	N0
	Human lung tumor SqCCa (SRCC738) [LT17]	IIB			T2	N1
	Human lung tumor SqCCa (SRCC739) [LT18]	IB			T2	N0
20	Human lung tumor SqCCa (SRCC740) [LT19]	IB			T2	N0
	Human lung tumor LCCa (SRCC741) [LT21]	IIB			T3	N1
	Human lung AdenoCa (SRCC811) [LT22]	1A			T1	N0
	Human colon AdenoCa (SRCC742) [CT2]		M1	D	pT4	N0
	Human colon AdenoCa (SRCC743) [CT3]			B	pT3	N0
25	Human colon AdenoCa (SRCC744) [CT8]			B	T3	N0
	Human colon AdenoCa (SRCC745) [CT10]			A	pT2	N0
	Human colon AdenoCa (SRCC746) [CT12]		MO, R1	B	T3	N0
	Human colon AdenoCa (SRCC747) [CT14]		pMO, RO	B	pT3	pN0
	Human colon AdenoCa (SRCC748) [CT15]		M1, R2	D	T4	N2
30	Human colon AdenoCa (SRCC749) [CT16]		pMO	B	pT3	pN0
	Human colon AdenoCa (SRCC750) [CT17]			C1	pT3	pN1
	Human colon AdenoCa (SRCC751) [CT1]		MO, R1	B	pT3	N0
	Human colon AdenoCa (SRCC752) [CT4]			B	pT3	M0
	Human colon AdenoCa (SRCC753) [CT5]		G2	C1	pT3	pN0
35	Human colon AdenoCa (SRCC754) [CT6]		pMO, RO	B	pT3	pN0
	Human colon AdenoCa (SRCC755) [CT7]		G1	A	pT2	pN0
	Human colon AdenoCa (SRCC756) [CT9]		G3	D	pT4	pN2
	Human colon AdenoCa (SRCC757) [CT11]			B	T3	N0
40	Human colon AdenoCa (SRCC758) [CT18]		MO, RO	B	pT3	pN0

#### DNA Preparation:

DNA was prepared from cultured cell lines, primary tumors, normal human blood. The isolation was performed using purification kit, buffer set and protease and all from Quiagen, according to the manufacturer's instructions and the description below.

#### *Cell culture lysis:*

Cells were washed and trypsinized at a concentration of  $7.5 \times 10^8$  per tip and pelleted by centrifuging at 1000 rpm for 5 minutes at 4°C, followed by washing again with 1/2 volume of PBS recentrifugation. The pellets were washed a third time, the suspended cells collected and washed 2x with PBS. The cells were then suspended into 10 ml PBS. Buffer C1 was equilibrated at 4°C. Qiagen protease #19155 was diluted into 6.25 ml cold ddH<sub>2</sub>O to a final concentration of 20 mg/ml and equilibrated at 4°C. 10 ml of G2 Buffer was prepared



by diluting Qiagen RNase A stock (100 mg/ml) to a final concentration of 200  $\mu$ g/ml.

Buffer C1 (10 ml, 4°C) and ddH<sub>2</sub>O (40 ml, 4°C) were then added to the 10 ml of cell suspension, mixed by inverting and incubated on ice for 10 minutes. The cell nuclei were pelleted by centrifuging in a Beckman swinging bucket rotor at 2500 rpm at 4°C for 15 minutes. The supernatant was discarded and the nuclei were suspended with a vortex into 2 ml Buffer C1 (at 4°C) and 6 ml ddH<sub>2</sub>O, followed by a second 4°C centrifugation at 2500 rpm for 15 minutes. The nuclei were then resuspended into the residual buffer using 200  $\mu$ l per tip. G2 buffer (10 ml) was added to the suspended nuclei while gentle vortexing was applied. Upon completion of buffer addition, vigorous vortexing was applied for 30 seconds. Quiagen protease (200  $\mu$ l, prepared as indicated above) was added and incubated at 50°C for 60 minutes. The incubation and centrifugation was repeated until the lysates were clear (*e.g.*, incubating additional 30-60 minutes, pelleting at 3000 x g for 10 min., 4°C).

*Solid human tumor sample preparation and lysis:*

Tumor samples were weighed and placed into 50 ml conical tubes and held on ice. Processing was limited to no more than 250 mg tissue per preparation (1 tip/preparation). The protease solution was freshly prepared by diluting into 6.25 ml cold ddH<sub>2</sub>O to a final concentration of 20 mg/ml and stored at 4°C. G2 buffer (20 ml) was prepared by diluting DNase A to a final concentration of 200 mg/ml (from 100 mg/ml stock). The tumor tissue was homogenated in 19 ml G2 buffer for 60 seconds using the large tip of the polytron in a laminar-flow TC hood in order to avoid inhalation of aerosols, and held at room temperature. Between samples, the polytron was cleaned by spinning at 2 x 30 seconds each in 2L ddH<sub>2</sub>O, followed by G2 buffer (50 ml). If tissue was still present on the generator tip, the apparatus was disassembled and cleaned. Quiagen protease (prepared as indicated above, 1.0 ml) was added, followed by vortexing and incubation at 50°C for 3 hours. The incubation and centrifugation was repeated until the lysates were clear (*e.g.*, incubating additional 30-60 minutes, pelleting at 3000 x g for 10 min., 4°C).

*Human blood preparation and lysis:*

Blood was drawn from healthy volunteers using standard infectious agent protocols and citrated into 10 ml samples per tip. Quiagen protease was freshly prepared by dilution into 6.25 ml cold ddH<sub>2</sub>O to a final concentration of 20 mg/ml and stored at 4°C. G2 buffer was prepared by diluting RNase A to a final concentration of 200  $\mu$ g/ml from 100 mg/ml stock. The blood (10 ml) was placed into a 50 ml conical tube and 10 ml C1 buffer and 30 ml ddH<sub>2</sub>O (both previously equilibrated to 4°C) were added, and the components mixed by inverting and held on ice for 10 minutes. The nuclei were pelleted with a Beckman swinging bucket rotor at 2500 rpm, 4°C for 15 minutes and the supernatant discarded. With a vortex, the nuclei were suspended into 2 ml C1 buffer (4°C) and 6 ml ddH<sub>2</sub>O (4°C). Vortexing was repeated until the pellet was white. The nuclei were then suspended into the residual buffer using a 200  $\mu$ l tip. G2 buffer (10 ml) were added to the suspended nuclei while gently vortexing, followed by vigorous vortexing for 30 seconds. Quiagen protease was added (200  $\mu$ l) and incubated at 50°C for 60 minutes. The incubation and centrifugation was repeated until the lysates were clear (*e.g.*, incubating additional 30-60 minutes, pelleting at 3000 x g for 10 min., 4°C).

*Purification of cleared lysates:*(1) Isolation of genomic DNA:

Genomic DNA was equilibrated (1 sample per maxi tip preparation) with 10 ml QBT buffer. QF elution buffer was equilibrated at 50°C. The samples were vortexed for 30 seconds, then loaded onto equilibrated tips and drained by gravity. The tips were washed with 2 x 15 ml QC buffer. The DNA was eluted into 30 ml silanized, autoclaved 30 ml Corex tubes with 15 ml QF buffer (50°C). Isopropanol (10.5 ml) was added to each sample, the tubes covered with parafilm and mixed by repeated inversion until the DNA precipitated. Samples were pelleted by centrifugation in the SS-34 rotor at 15,000 rpm for 10 minutes at 4°C. The pellet location was marked, the supernatant discarded, and 10 ml 70% ethanol (4°C) was added. Samples were pelleted again by centrifugation on the SS-34 rotor at 10,000 rpm for 10 minutes at 4°C. The pellet location was marked and the supernatant discarded. The tubes were then placed on their side in a drying rack and dried 10 minutes at 37°C, taking care not to overdry the samples.

After drying, the pellets were dissolved into 1.0 ml TE (pH 8.5) and placed at 50°C for 1-2 hours. Samples were held overnight at 4°C as dissolution continued. The DNA solution was then transferred to 1.5 ml tubes with a 26 gauge needle on a tuberculin syringe. The transfer was repeated 5x in order to shear the DNA. Samples were then placed at 50°C for 1-2 hours.

(2) Quantitation of genomic DNA and preparation for gene amplification assay:

The DNA levels in each tube were quantified by standard  $A_{260}$ ,  $A_{280}$  spectrophotometry on a 1:20 dilution (5  $\mu$ l DNA + 95  $\mu$ l ddH<sub>2</sub>O) using the 0.1 ml quartz cuvetts in the Beckman DU640 spectrophotometer.  $A_{260}/A_{280}$  ratios were in the range of 1.8-1.9. Each DNA sample was then diluted further to approximately 200 ng/ml in TE (pH 8.5). If the original material was highly concentrated (about 700 ng/ $\mu$ l), the material was placed at 50°C for several hours until resuspended.

Fluorometric DNA quantitation was then performed on the diluted material (20-600 ng/ml) using the manufacturer's guidelines as modified below. This was accomplished by allowing a Hoeffer DyNA Quant 200 fluorometer to warm-up for about 15 minutes. The Hoechst dye working solution (#H33258, 10  $\mu$ l, prepared within 12 hours of use) was diluted into 100 ml 1 x TNE buffer. A 2 ml cuvette was filled with the fluorometer solution, placed into the machine, and the machine was zeroed. pGEM 3Zf(+) (2  $\mu$ l, lot #360851026) was added to 2 ml of fluorometer solution and calibrated at 200 units. An additional 2  $\mu$ l of pGEM 3Zf(+) DNA was then tested and the reading confirmed at 400 +/- 10 units. Each sample was then read at least in triplicate. When 3 samples were found to be within 10% of each other, their average was taken and this value was used as the quantification value.

The fluorometrically determined concentration was then used to dilute each sample to 10 ng/ $\mu$ l in ddH<sub>2</sub>O. This was done simultaneously on all template samples for a single TaqMan plate assay, and with enough material to run 500-1000 assays. The samples were tested in triplicate with Taqman™ primers and probe both B-actin and GAPDH on a single plate with normal human DNA and no-template controls. The diluted samples were used provided that the CT value of normal human DNA subtracted from test DNA was +/- 1 Ct. The diluted, lot-qualified genomic DNA was stored in 1.0 ml aliquots at -80°C. Aliquots which were subsequently to be used in the gene amplification assay were stored at 4°C. Each 1 ml aliquot is enough

for 8-9 plates or 64 tests.

*Gene amplification assay:*

The PRO polypeptide compounds of the invention were screened in the following primary tumors and the resulting  $\Delta C_t$  values greater than or equal to 1.0 are reported in Tables 9A-C below.

Table 9A

<u><math>\Delta</math>Ct values in lung and colon primary tumors and cell line models</u>									
Primary Tumor	PRO290	PRO341	PRO535	PRO619	PRO1112	PRO809	PRO830	PRO848	
LT-1a	—	—	—	—	—	—	1.13	—	—
LT3	—	—	—	1.04	—	—	—	—	—
				1.68					
LT7	—	—	—	1.21	—	—	—	—	—
				1.34					
LT9	—	—	—	1.19	—	—	—	—	—
				1.34					
LT10	—	—	—	1.41	1.135	—	—	—	—
				2.02					
LT11	1.63	—	1.40	1.69	1.525	1.40	1.25	1.04	—
				1.57					
LT12	—	—	—	1.81	1.195	1.61	1.35	1.22	—
LT13	1.47	—	1.37	2.13	1.635	1.03	—	—	—
				1.74					
LT15	1.67	—	—	2.08	1.775	—	—	—	—
				1.52					
LT16	—	1.12	—	—	—	—	—	—	—
LT17	1.22	1.33	1.42	1.83	1.455	1.10	1.17	—	—
				1.67					
LT18	—	—	—	1.32	1.255	—	—	—	—
				1.14					
LT19	2.07	—	—	2.33	—	—	1.31	—	—
				1.90					
LT21	—	1.15	—	1.15	—	1.05	—	1.07	—
				1.09					
CT2	1.56	—	—	1.22	2.265	—	—	—	—

Table 9A (cont')  
 $\Delta$ Ct values in lung and colon primary tumors and cell line models

Primary Tumor	PRO290	PRO341	PRO535	PRO619	PRO1112	PRO809	PRO830	PRO848
CT3	---	---	1.28	1.49	---	---	---	---
CT8	---	---	---	---	1.065	---	---	---
CT10	---	---	1.34	---	1.575	---	---	---
CT12	---	---	---	---	1.315	---	---	---
CT14	---	---	1.29	---	1.895	---	---	---
CT15	---	---	1.10	1.00	1.465	---	---	---
CT16	---	---	1.35	1.02	1.255	---	---	---
CT17	---	---	1.26	1.23	---	---	---	---
CT1	---	---	---	1.12	1.245	---	---	---
CT4	---	---	1.03	1.25	1.535	---	---	---
CT5	---	---	---	1.34	1.975	---	---	---
CT6	---	---	1.00	1.06	1.575	---	---	---
CT11	1.16	---	1.25	1.80	2.285	---	---	---

Table 9B

 $\Delta$ Ct values in lung and colon primary tumors and cell line models

Primary Tumor	PRO943	PRO1005	PRO1009	PRO1185	PRO1245	PRO1097	PRO1107	PRO1111	PRO1153
LT-1	---	1.07	---	---	---	---	---	---	---
LT-1a	---	3.87	---	---	---	---	---	---	---
LT2	---	---	---	---	---	1.23	---	---	---
LT3	---	1.61	---	1.01	---	---	---	1.39	---
LT4	---	---	---	---	---	---	---	1.49	1.01
LT6	---	1.29	---	---	---	---	---	---	---
LT7	---	---	---	---	---	---	---	1.58	1.52
LT9	---	2.50	---	---	---	1.21	---	1.44	---
LT10	---	---	---	---	---	---	---	1.05	---
LT11	2.06	---	---	---	---	---	---	1.45	---
LT12	1.94	1.21	---	---	---	---	---	---	---
LT13	1.64	2.30	---	---	3.84	---	3.55	---	---
LT15	2.05	1.03	---	---	1.01	---	2.47	---	---
LT16	---	1.05	---	---	1.98	---	2.45	---	---
LT17	1.93	---	---	---	---	---	---	1.47	---
LT19	2.90	---	---	---	---	---	---	---	---
LT26	---	---	---	1.66	---	---	---	---	---
LT30	---	---	---	1.58	---	---	---	---	---
CT2	1.92	---	2.00	1.73	---	---	4.75	---	---
CT3	---	---	1.75	---	---	---	1.52	---	---
CT8	1.37	---	1.29	---	---	---	---	---	---
	1.12								

Table 9B (cont')

 $\Delta$ Ct values in lung and colon primary tumors and cell line models

Primary Tumor	PRO943	PRO1005	PRO1009	PRO1185	PRO1245	PRO1097	PRO1107	PRO1111	PRO1153
CT10	2.13	---	1.73	---	---	---	2.82	---	---
	1.67								
CT12	1.43	---	1.92	---	---	---	---	---	---
CT14	1.46	---	2.10	---	---	1.08	1.54	1.38	---
CT15	---	---	2.02	---	1.00	---	---	---	---
CT16	---	---	1.56	---	---	1.11	---	---	---
CT17	1.30	---	1.76	---	---	1.34	---	---	---
CT1	1.36	---	---	---	---	---	1.57	---	---
CT4	---	---	1.06	---	---	---	1.59	---	---
CT5	1.88	---	1.43	---	---	---	---	---	---
	2.51								
CT6	1.41	---	---	---	---	---	---	---	---
	1.75								
CT7	---	---	---	---	---	---	---	1.16	---
CT11	2.80	---	1.83	---	---	---	---	1.17	---
	2.61								
CT18	1.30	---	---	---	---	---	---	1.05	---
H522	---	---	---	---	1.10	---	---	---	---

Table 9C

 $\Delta$ Ct values in lung and colon primary tumors and cell line models

	Primary Tumor	PRO1182	PRO1184	PRO1187	PRO1281
5	LT-1	1.81	---	---	---
	LT-1a	---	1.14	---	---
			1.09		
10	LT4	1.43	1.37	---	---
			1.18		
	LT6	---	1.78	---	---
15			1.66		
			1.05		
	LT9	1.43	---	---	---
20	LT12	---	2.47	1.17	---
			2.61		
			1.80		
25	LT15	---	---	1.55	---
	LT16	---	1.01	1.33	---
	LT17	---	---	---	---
30	LT18	---	1.07	---	---
			1.13		
	LT19	---	1.19	---	---
			1.35		
			1.02		
	LT21	---	1.00	---	---
			1.20		
	CT2	---	---	---	1.15
	CT12	---	---	---	1.07



Because amplification of the various DNAs described above occurs in various cancerous tumors and tumor cell lines derived from various human tissues, these molecules likely play a significant role in tumor formation and/or growth. As a result, amplification and/or enhanced expression of these molecules can serve as a diagnostic for detecting the presence of tumor in an individual and antagonists (*e.g.*, antibodies) directed against the proteins encoded by the above described DNA molecules would be expected to have utility in cancer therapy.

#### EXAMPLE 171: Identification of Receptor/Ligand Interactions

In this assay, various PRO polypeptides are tested for ability to bind to a panel of potential receptor molecules for the purpose of identifying receptor/ligand interactions. The identification of a ligand for a known receptor, a receptor for a known ligand or a novel receptor/ligand pair is useful for a variety of indications including, for example, targeting bioactive molecules (linked to the ligand or receptor) to a cell known to express the receptor or ligand, use of the receptor or ligand as a reagent to detect the presence of the ligand or receptor in a composition suspected of containing the same, wherein the composition may comprise cells suspected of expressing the ligand or receptor, modulating the growth of or another biological or immunological activity of a cell known to express or respond to the receptor or ligand, modulating the immune response of cells or toward cells that express the receptor or ligand, allowing the preparation of agonists, antagonists and/or antibodies directed against the receptor or ligand which will modulate the growth of or a biological or immunological activity of a cell expressing the receptor or ligand, and various other indications which will be readily apparent to the ordinarily skilled artisan.

The assay is performed as follows. A PRO polypeptide of the present invention suspected of being a ligand for a receptor is expressed as a fusion protein containing the Fc domain of human IgG (an immunoadhesin). Receptor-ligand binding is detected by allowing interaction of the immunoadhesin polypeptide with cells (*e.g.* Cos cells) expressing candidate PRO polypeptide receptors and visualization of bound immunoadhesin with fluorescent reagents directed toward the Fc fusion domain and examination by microscope. Cells expressing candidate receptors are produced by transient transfection, in parallel, of defined subsets of a library of cDNA expression vectors encoding PRO polypeptides that may function as receptor molecules. Cells are then incubated for 1 hour in the presence of the PRO polypeptide immunoadhesin being tested for possible receptor binding. The cells are then washed and fixed with paraformaldehyde. The cells are then incubated with fluorescent conjugated antibody directed against the Fc portion of the PRO polypeptide immunoadhesin (*e.g.* FITC conjugated goat anti-human-Fc antibody). The cells are then washed again and examined by microscope. A positive interaction is judged by the presence of fluorescent labeling of cells transfected with cDNA encoding a particular PRO polypeptide receptor or pool of receptors and an absence of similar fluorescent labeling of similarly prepared cells that have been transfected with other cDNA or pools of cDNA. If a defined pool of cDNA expression vectors is judged to be positive for interaction with a PRO polypeptide immunoadhesin, the individual cDNA species that comprise the pool are tested individually (the pool is "broken down") to determine the specific cDNA that encodes a receptor able to interact with the PRO polypeptide immunoadhesin.

In another embodiment of this assay, an epitope-tagged potential ligand PRO polypeptide (e.g. histidine "His" tag) is allowed to interact with a panel of potential receptor PRO polypeptide molecules that have been expressed as fusions with the Fc domain of human IgG (immunoadhesins). Following a 1 hour co-incubation with the epitope tagged PRO polypeptide, the candidate receptors are each immunoprecipitated with protein A beads and the beads are washed. Potential ligand interaction is determined by western blot analysis of the immunoprecipitated complexes with antibody directed towards the epitope tag. An interaction is judged to occur if a band of the anticipated molecular weight of the epitope tagged protein is observed in the western blot analysis with a candidate receptor, but is not observed to occur with the other members of the panel of potential receptors.

Using these assays, the following receptor/ligand interactions have been herein identified:

- (1) PRO943 binds to FHF1, PRO183 (FHF2), PRO184 (FHF3) and PRO185 (FHF4) and vice versa.
- (2) PRO331 binds to PRO1133 and vice versa.
- (3) PRO363 binds to PRO1387 and vice versa.
- (4) PRO5723 binds to PRO1387 and vice versa.
- (5) PRO1114 binds to PRO3301 and PRO9940 and vice versa.
- (6) PRO9828 appears to be a novel fibroblast growth factor receptor (FGFR) ligand in that it binds to the known FGF receptors FGFR1, FGFR2IIIC, FGFR3IIIC and FGFR4. PRO9828 and agonists, therefore, will find use for activating the biological activities normally activated by FGF molecules including, for example, cell growth and proliferation. Antagonists of PRO9828 will find use in blocking the biological activities mediated through the FGF receptor.
- (7) PRO1181 binds to PRO7170, PRO361 and PRO846.

#### EXAMPLE 172: Tissue Expression Distribution

Oligonucleotide probes were constructed from the PRO polypeptide-encoding nucleotide sequences shown in the figures for use in quantitative PCR amplification reactions. The oligonucleotide probes were chosen so as to give an approximately 200-600 base pair amplified fragment from the 3' end of its associated template in a standard PCR reaction. The oligonucleotide probes were employed in standard quantitative PCR amplification reactions with cDNA libraries isolated from different human adult and/or fetal tissue sources and analyzed by agarose gel electrophoresis so as to obtain a quantitative determination of the level of expression of the PRO polypeptide-encoding nucleic acids in the various tissues tested. Knowledge of the expression pattern or the differential expression of the PRO polypeptide-encoding nucleic acids in various different human tissue types provides a diagnostic marker useful for tissue typing, with or without other tissue-specific markers, for determining the primary tissue source of a metastatic tumor, disease diagnosis, and the like. These assays provided the following results.

<u>DNA Molecule</u>	<u>Tissues w/ Significant Expression</u>	<u>Tissues w/o Significant Expression</u>
DNA16422-1209	substantia nigra, dendrocytes, uterus	hippocampus
DNA16435-1208	substantia nigra, dendrocytes, uterus	hippocampus
DNA26843-1389	dendrocytes, heart, uterus, colon tumor	hippocampus, substantia nigra, cartilage

	<u>DNA Molecule</u>	<u>Tissues w/ Significant Expression</u>	<u>Tissues w/o Significant Expression</u>
	DNA26844-1394	HUVEC, dendrocytes, cartilage	substantia nigra, hippocampus, uterus, prostate
5	DNA40621-1440 DNA44161-1434	prostate, uterus, colon tumor colon tumor, dendrocytes	brain, heart, HUVEC, cartilage substantia nigra, hippocampus, prostate, uterus
	DNA44694-1500	dendrocytes, hippocampus, prostate	colon tumor, substantia nigra, heart
	DNA48320-1433	prostate, uterus	colon tumor, brain, heart, cartilage
	DNA49647-1398	brain, heart, prostate, uterus	cartilage
10	DNA53913-1490	hippocampus	substantia nigra, dendrocytes
	DNA53978-1443	dendrocytes, uterus, prostate	substantia nigra, colon tumor
	DNA53996-1442	spleen, prostate, uterus, hippocampus	substantia nigra, heart
	DNA56050-1455	prostate, uterus, cartilage, hippocampus	heart, colon tumor, dendrocytes
	DNA56110-1437	spleen, colon tumor, brain, prostate	heart
15	DNA56410-1414	uterus, dendrocytes	hippocampus, substantia nigra, heart
	DNA56436-1448	substantia nigra, prostate, hippocampus	dendrocytes, heart, HUVEC
	DNA56855-1447	prostate, uterus	brain, cartilage, heart, colon tumor
	DNA56860-1510	colon tumor	prostate, uterus, dendrocytes
	DNA56868-1478	colon tumor, prostate	uterus, brain, heart, cartilage
20	DNA56869-1545	prostate, uterus, cartilage	brain, colon tumor, spleen, heart
	DNA57699-1412	dendrocytes, hippocampus, prostate	substantia nigra, heart
	DNA57704-1452	brain, heart, spleen, uterus, prostate	colon tumor
	DNA57710-1451	dendrocytes, hippocampus, spleen, uterus	substantia nigra, heart
	DNA57711-1501	dendrocytes, hippocampus, heart, cartilage	substantia nigra
25	DNA57827-1493	colon tumor, hippocampus, prostate	substantia nigra, dendrocytes, uterus
	DNA58723-1588	substantia nigra, cartilage uterus	hippocampus, dendrocytes, HUVEC
	DNA58743-1609	brain, prostate, uterus	colon tumor, heart, spleen, cartilage
	DNA58846-1409	hippocampus, dendrocytes	substantia nigra, uterus, prostate, colon tumor
30	DNA58849-1494	prostate	brain, uterus, cartilage, heart, colon tumor
	DNA58850-1495	spleen, prostate, dendrocytes	hippocampus, substantia nigra, colon tumor
35	DNA59213-1487	spleen, cartilage, prostate, substantia nigra	heart, hippocampus, dendrocytes
	DNA59497-1496	dendrocytes, prostate, uterus, heart	cartilage, hippocampus, substantia nigra
	DNA59605-1418	dendrocytes, prostate, uterus	hippocampus, substantia nigra, colon tumor
	DNA59609-1470	dendrocytes	substantia nigra, hippocampus, heart, prostate, uterus, spleen
40	DNA59612-1466	prostate, dendrocytes	hippocampus, substantia nigra, uterus, colon tumor
	DNA59616-1465	dendrocytes, substantia nigra, colon tumor	hippocampus
	DNA59619-1464	dendrocytes, substantia nigra, colon tumor	hippocampus
45	DNA59625-1498	brain, colon tumor, prostate, uterus	THP-1 macrophages
	DNA59827-1426	substantia nigra, prostate, uterus	hippocampus, dendrocytes, heart
	DNA59828-1608	dendrocytes, substantia nigra, colon tumor	hippocampus
	DNA59853-1505	prostate	brain, uterus, spleen, heart, colon tumor
50	DNA59854-1459	cartilage	prostate, brain, heart, colon tumor
	DNA60283-1484	dendrocytes, spleen, prostate, uterus	hippocampus, substantia nigra, heart
	DNA60619-1482	dendrocytes, substantia nigra, colon tumor	hippocampus
	DNA60625-1507	cartilage	prostate, brain, heart, colon tumor
	DNA60629-1481	uterus, colon tumor, substantia nigra	hippocampus, dendrocytes, spleen, prostate
55	DNA61755-1554	dendrocytes, substantia nigra, colon tumor	hippocampus

<u>DNA Molecule</u>	<u>Tissues w/ Significant Expression</u>	<u>Tissues w/o Significant Expression</u>
DNA64852-1589	prostate, uterus	brain, heart, cartilage, colon tumor
DNA66308-1537	prostate, heart uterus	brain, colon tumor, cartilage
DNA68869-1610	spleen, prostate, heart, uterus, colon tumor, substantia nigra	hippocampus, dendrocytes, prostate

5

EXAMPLE 173: Isolation of cDNA Clones Encoding Human PRO846

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA39949. Based on the DNA39949 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO846.

10

Forward and reverse PCR primers were synthesized:

forward PCR primer 5'-CCCTGCAGTGCACCTACAGGGAAG-3' (SEQ ID NO:518)

reverse PCR primer 5'-CTGTCTTCCCCTGCTTGGCTGTGG-3' (SEQ ID NO:519)

15

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA39949 sequence which had the following nucleotide sequence

hybridization probe

5'-GGTGCAGGAAGGGTGGGATCCTCTTCTCTCGCTGCTCTGGCCACATC-3'

(SEQ ID NO:520)

20

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO846 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

25

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO846 [herein designated as DNA44196-1353] (SEQ ID NO:516) and the derived protein sequence for PRO846.

30

The entire nucleotide sequence of UNQ422 (DNA44196-1353) is shown in Figure 329 (SEQ ID NO:516). Clone UNQ422 (DNA44196-1353) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 25-27 and ending at the stop codon at nucleotide positions 1021-1023 (Figure 329). The predicted polypeptide precursor is 332 amino acids long (Figure 330). The full-length PRO846 protein shown in Figure 330 has an estimated molecular weight of about 36,143 daltons and a pI of about 5.89. Important regions of the amino acid sequence of PRO846 include the signal peptide, the transmembrane domain, an N-glycosylation site, a sequence typical of fibrinogen beta and gamma chains C-terminal domain, and a sequence typical of Ig like V-type domain as shown in Figure 330. Clone UNQ422 (DNA44196-1353) has been deposited with ATCC and is assigned ATCC deposit no. 209847.

35

EXAMPLE 174: Isolation of cDNA Clones Encoding Human PRO363

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA42828. Based on the DNA42828 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO363.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer (42828.f1) 5'-CCAGTGCACAGCAGGCAACGAAGC-3' (SEQ ID NO:521)

reverse PCR primer (42828.r1) 5'-ACTAGGCTGTATGCCTGGGTGGGC-3' (SEQ ID NO:522)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA42828 sequence which had the following nucleotide sequence

hybridization probe (42828.p1)

5'-GTATGTACAAAGCATCGGCATGGTTGCAGGAGCAGTGACAGGC-3' (SEQ ID NO:523)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO363 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO363 [herein designated as UNQ318 (DNA45419-1252)] (SEQ ID NO:500) and the derived protein sequence for PRO363.

The entire nucleotide sequence of UNQ318 (DNA45419-1252) is shown in Figure 313 (SEQ ID NO:500). Clone UNQ318 (DNA45419-1252) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 190-192 and ending at the stop codon at nucleotide positions 1309-1311 (Figure 313). The predicted polypeptide precursor is 373 amino acids long (Figure 314). The full-length PRO363 protein shown in Figure 314 has an estimated molecular weight of about 41,281 daltons and a pI of about 8.33. A transmembrane domain exists at amino acids 221 to 254 of the amino acid sequence shown in Figure 314 (SEQ ID NO:501). The PRO363 polypeptide also possesses at least two myelin P0 protein domains from about amino acids 15 to 56 and from about amino acids 87 to 116. Clone UNQ318 (DNA45419-1252) has been deposited with ATCC on February 5, 1998 and is assigned ATCC deposit no. 209616.

Analysis of the amino acid sequence of the full-length PRO363 polypeptide suggests that it possesses significant sequence similarity to the cell surface protein HCAR, thereby indicating that PRO363 may be a novel HCAR homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO363 amino acid sequence and the following Dayhoff sequences, HS46KDA\_1, HSU90716\_1, MMCARH\_1, MMCARHOM\_1, MMU90715\_1, A33\_HUMAN, P\_W14146, P\_W14158, A42632 and B42632.

EXAMPLE 175: Isolation of cDNA Clones Encoding a Human PRO9828

A consensus DNA sequence was assembled relative to other nucleic sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA139814. Based on the DNA139814 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO9828. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, *supra*, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

5'-AATCTCAGCACCAGCCACTCAGAGCA-3' (SEQ ID NO:524)

5'-GTAAAGAGGGTGCCCTTCCAGCGA-3' (SEQ ID NO:525)

5'-TATCCCAATGCCTCCCCACTGCTC-3' (SEQ ID NO:526)

5'-GATGAAGTTGGCGAAGGGGCGGCA-3' (SEQ ID NO:527)

RNA for construction of the cDNA libraries was isolated from human fetal liver tissue. The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for a full-length PRO9828 polypeptide (designated herein as DNA142238-2768 [Figure 323, SEQ ID NO:510]) and the derived protein sequence for that PRO9828 polypeptide.

The full length clone identified above contained a single open reading frame with an apparent translational initiation site at nucleotide positions 232-234 and a stop signal at nucleotide positions 985-987 (Figure 323, SEQ ID NO:510). The predicted polypeptide precursor is 251 amino acids long, has a calculated molecular weight of approximately 27,954 daltons and an estimated pI of approximately 9.22. Analysis of the full-length PRO9828 sequence shown in Figure 324 (SEQ ID NO:511) evidences the presence of a variety of important polypeptide domains as shown in Figure 324, wherein the locations given for those important polypeptide domains are approximate as described above. Chromosome mapping evidences that the PRO9828-encoding nucleic acid maps to chromosome 12p13 in humans. Clone DNA142238-2768 has been deposited with ATCC on October 5, 1999 and is assigned ATCC deposit no. 819-PTA.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using the ALIGN-2 sequence alignment analysis of the full-length sequence shown in Figure 324 (SEQ ID NO:511), evidenced sequence

identity between the PRO9828 amino acid sequence and the following Dayhoff sequences: P\_Y08581, AB018122\_1, FGF3\_HUMAN, P\_R70824, S54407, P\_R80780, P\_Y23761, P\_W92312, OMFGF6\_1 and P\_R80871.

EXAMPLE 176: Isolation of cDNA Clones Encoding a Human PRO7170

5 DNA108722-2743 was identified by applying a proprietary signal sequence finding algorithm developed by Genentech, Inc. (South San Francisco, CA) upon ESTs as well as clustered and assembled EST fragments from public (e.g., Genbank) and/or private (LIFESEQ®, Incyte Pharmaceuticals, Inc., Palo Alto, CA) databases. The signal sequence algorithm computes a secretion signal score based on the character of the DNA nucleotides surrounding the first and optionally the second methionine codon(s) (ATG) at the 5'-end of the sequence or sequence fragment under consideration. The nucleotides following the first ATG must code for at least 35 unambiguous amino acids without any stop codons. If the first ATG has the required amino acids, the second is not examined. If neither meets the requirement, the candidate sequence is not scored. In order to determine whether the EST sequence contains an authentic signal sequence, the DNA and corresponding amino acid sequences surrounding the ATG codon are scored using a set of seven sensors (evaluation parameters) known to be associated with secretion signals.

15 Use of the above described signal sequence algorithm allowed identification of an EST cluster sequence from the LIFESEQ® database, Incyte Pharmaceuticals, Palo Alto, designated herein as CLU57836. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., Genbank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA58756.

25 In light of an observed sequence homology between the DNA58756 sequence and an EST sequence encompassed within clone no. 2251462 from the LIFESEQ® database, Incyte Pharmaceuticals, Palo Alto, CA, clone no. 2251462 was purchased and the cDNA insert was obtained and sequenced. It was found herein that that cDNA insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 325 and is herein designated as DNA108722-2743.

30 Clone DNA108722-2743 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 60-62 and ending at the stop codon at nucleotide positions 1506-1508 (Figure 325). The predicted polypeptide precursor is 482 amino acids long (Figure 326). The full-length PRO7170 protein shown in Figure 326 has an estimated molecular weight of about 49,060 daltons and a pI of about 4.74. Analysis of the full-length PRO7170 sequence shown in Figure 326 (SEQ ID NO:513) evidences the presence of a variety of important polypeptide domains as shown in Figure 326, wherein the locations given for those important polypeptide domains are approximate as described above. Clone DNA108722-2743 has been

deposited with ATCC on August 17, 1999 and is assigned ATCC Deposit No. 552-PTA.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using the ALIGN-2 sequence alignment analysis of the full-length sequence shown in Figure 326 (SEQ ID NO:513), evidenced sequence identity between the PRO7170 amino acid sequence and the following Dayhoff sequences: P\_Y12291, I47141, D88733\_1, DMC56G7\_1, P\_Y11606, HWP1\_CANAL, HSMUC5BEX\_1, HSU78550\_1, HSU70136\_1, and SGS3\_DROME.

#### EXAMPLE 177: Isolation of cDNA Clones Encoding Human PRO361

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA40654. Based on the DNA40654 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO361.

Forward and reverse PCR primers were synthesized as follows:

<u>forward PCR primer</u>	5'-AGGGAGGATTATCCTTGACCTTTGAAGACC-3'	(SEQ ID NO:528)
<u>forward PCR primer</u>	5'-GAAGCAAGTGCCCAGCTC-3'	(SEQ ID NO:529)
<u>forward PCR primer</u>	5'-CGGGTCCCTGCTCTTTGG-3'	(SEQ ID NO:530)
<u>reverse PCR primer</u>	5'-CACCGTAGCTGGGAGCGCACTCAC-3'	(SEQ ID NO:531)
<u>reverse PCR primer</u>	5'-AGTGTAAGTCAAGCTCCC-3'	(SEQ ID NO:532)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40654 sequence which had the following nucleotide sequence

#### hybridization probe

5'- GCTTCCTGACACTAAGGCTGTCTGCTAGTCAGAATTGCCTCAAAAAGAG-3' (SEQ ID NO:533)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO361 gene using the probe oligonucleotide. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO361 [herein designated as DNA45410-1250] (SEQ ID NO:514) and the derived protein sequence for PRO361.

The entire nucleotide sequence of DNA45410-1250 is shown in Figure 327 (SEQ ID NO:514). Clone DNA45410-1250 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 226-228 and ending at the stop codon at nucleotide positions 1519-1521 (Figure 327). The predicted polypeptide precursor is 431 amino acids long (Figure 328). The full-length PRO361 protein shown in Figure 328 has an estimated molecular weight of about 46,810 daltons and a pI of about 6.45. In addition, regions of interest including the transmembrane domain (amino acids 380-409) and sequences typical of the arginase family of proteins (amino acids 3-14 and 39-57) are designated in Figure 328. Clone DNA45410-1250 has been deposited with ATCC and is assigned ATCC deposit no. ATCC 209621.



Analysis of the amino acid sequence of the full-length PRO361 polypeptide suggests that portions of it possess significant homology to the mucin and/or chitinase proteins, thereby indicating that PRO361 may be a novel mucin and/or chitinase protein.

EXAMPLE 178: Isolation of cDNA Clones Encoding a Human PRO183, PRO184, PRO185, PRO5723,

PRO3301 or PRO9940

DNA molecules encoding the PRO183, PRO184, PRO185, PRO5723, PRO3301 or PRO9940 polypeptides shown in the accompanying figures were obtained through GenBank.

Deposit of Material

The following materials have been deposited with the American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209, USA (ATCC):

Table 10

	<u>Material</u>	<u>ATCC Dep. No.</u>	<u>Deposit Date</u>
15	DNA45410-1250	209621	February 5, 1998
	DNA108722-2743	552-PTA	August 17, 1999
	DNA142238-2768	819-PTA	October 5, 1999
	DNA40981-1234	209439	November 7, 1997
	DNA45419-1252	209616	February 5, 1998
20	DNA44196-1353	209847	May 6, 1998
	DNA16422-1209	209929	June 2, 1998
	DNA16435-1208	209930	June 2, 1998
	DNA21624-1391	209917	June 2, 1998
	DNA23334-1392	209918	June 2, 1998
25	DNA26288-1239	209792	April 21, 1998
	DNA26843-1389	203099	August 4, 1998
	DNA26844-1394	209926	June 2, 1998
	DNA30862-1396	209920	June 2, 1998
	DNA35680-1212	209790	April 21, 1998
30	DNA40621-1440	209922	June 2, 1998
	DNA44161-1434	209907	May 27, 1998
	DNA44694-1500	203114	August 11, 1998
	DNA45495-1550	203156	August 25, 1998
	DNA47361-1154	209431	November 7, 1997
35	DNA47394-1572	203109	August 11, 1998
	DNA48320-1433	209904	May 27, 1998
	DNA48334-1435	209924	June 2, 1998
	DNA48606-1479	203040	July 1, 1998
	DNA49141-1431	203003	June 23, 1998
40	DNA49142-1430	203002	June 23, 1998
	DNA49143-1429	203013	June 23, 1998
	DNA49647-1398	209919	June 2, 1998
	DNA49819-1439	209931	June 2, 1998
	DNA49820-1427	209932	June 2, 1998
45	DNA49821-1562	209981	June 16, 1998
	DNA52192-1369	203042	July 1, 1998
	DNA52598-1518	203107	August 11, 1998
	DNA53913-1490	203162	August 25, 1998

Table 10 (cont')

	DNA53978-1443	209983	June 16, 1998
	DNA53996-1442	209921	June 2, 1998
	DNA56041-1416	203012	June 23, 1998
	DNA56047-1456	209948	June 9, 1998
5	DNA56050-1455	203011	June 23, 1998
	DNA56110-1437	203113	August 11, 1998
	DNA56113-1378	203049	July 1, 1998
	DNA56410-1414	209923	June 2, 1998
	DNA56436-1448	209902	May 27, 1998
10	DNA56855-1447	203004	June 23, 1998
	DNA56859-1445	203019	June 23, 1998
	DNA56860-1510	209952	June 9, 1998
	DNA56865-1491	203022	June 23, 1998
	DNA56866-1342	203023	June 23, 1998
15	DNA56868-1209	203024	June 23, 1998
	DNA56869-1545	203161	August 25, 1998
	DNA56870-1492	209925	June 2, 1998
	DNA57033-1403	209905	May 27, 1998
	DNA57037-1444	209903	May 27, 1998
20	DNA57129-1413	209977	June 16, 1998
	DNA57690-1374	209950	June 9, 1998
	DNA57693-1424	203008	June 23, 1998
	DNA57694-1341	203017	June 23, 1998
	DNA57695-1340	203006	June 23, 1998
25	DNA57699-1412	203020	June 23, 1998
	DNA57702-1476	209951	June 9, 1998
	DNA57704-1452	209953	June 9, 1998
	DNA57708-1411	203021	June 23, 1998
	DNA57710-1451	203048	July 1, 1998
30	DNA57711-1501	203047	July 1, 1998
	DNA57827-1493	203045	July 1, 1998
	DNA57834-1339	209954	June 9, 1998
	DNA57836-1338	203025	June 23, 1998
	DNA57838-1337	203014	June 23, 1998
35	DNA57844-1410	203010	June 23, 1998
	DNA58721-1475	203110	August 11, 1998
	DNA58723-1588	203133	August 18, 1998
	DNA58737-1473	203136	August 18, 1998
	DNA58743-1609	203154	August 25, 1998
40	DNA58846-1409	209957	June 9, 1998
	DNA58848-1472	209955	June 9, 1998
	DNA58849-1494	209958	June 9, 1998
	DNA58850-1495	209956	June 9, 1998
	DNA58853-1423	203016	June 23, 1998
45	DNA58855-1422	203018	June 23, 1998
	DNA59205-1421	203009	June 23, 1998
	DNA59211-1450	209960	June 9, 1998
	DNA59213-1487	209959	June 9, 1998
	DNA59214-1449	203046	July 1, 1998
50	DNA59215-1425	209961	June 9, 1998
	DNA59220-1514	209962	June 9, 1998
	DNA59488-1603	203157	August 25, 1998
	DNA59493-1420	203050	July 1, 1998
	DNA59497-1496	209941	June 4, 1998
55	DNA59588-1571	203106	August 11, 1998

Table 10 (cont')

	DNA59603-1419	209944	June 9, 1998
	DNA59605-1418	203005	June 23, 1998
	DNA59606-1471	209945	June 9, 1998
	DNA59607-1497	209957	June 9, 1998
5	DNA59609-1470	209963	June 9, 1998
	DNA59610-1559	209990	June 16, 1998
	DNA59612-1466	209947	June 9, 1998
	DNA59613-1417	203007	June 23, 1998
	DNA59616-1465	209991	June 16, 1998
10	DNA59619-1464	203041	July 1, 1998
	DNA59620-1463	209989	June 16, 1998
	DNA59625-1498	209992	June 17, 1998
	DNA59767-1489	203108	August 11, 1998
	DNA59776-1600	203128	August 18, 1998
15	DNA59777-1480	203111	August 11, 1998
	DNA59820-1549	203129	August 18, 1998
	DNA59827-1426	203089	August 4, 1998
	DNA59828-1608	203158	August 25, 1998
	DNA59838-1462	209976	June 16, 1998
20	DNA59839-1461	209988	June 16, 1998
	DNA59841-1460	203044	July 1, 1998
	DNA59842-1502	209982	June 16, 1998
	DNA59846-1503	209978	June 16, 1998
	DNA59847-1511	203098	August 4, 1998
25	DNA59848-1512	203088	August 4, 1998
	DNA59849-1504	209986	June 16, 1998
	DNA59853-1505	209985	June 16, 1998
	DNA59854-1459	209974	June 16, 1998
	DNA60283-1484	203043	July 1, 1998
30	DNA60615-1483	209980	June 16, 1998
	DNA60619-1482	209993	June 16, 1998
	DNA60621-1516	203091	August 4, 1998
	DNA60622-1525	203090	August 4, 1998
	DNA60625-1507	209975	June 16, 1998
35	DNA60627-1508	203092	August 4, 1998
	DNA60629-1481	209979	June 16, 1998
	DNA61755-1554	203112	August 11, 1998
	DNA61873-1574	203132	August 18, 1998
	DNA62814-1521	203093	August 4, 1998
40	DNA62872-1509	203100	August 4, 1998
	DNA62876-1517	203095	August 4, 1998
	DNA62881-1515	203096	August 4, 1998
	DNA64852-1589	203127	August 18, 1998
	DNA64884-1527	203155	August 25, 1998
45	DNA64890-1612	203131	August 18, 1998
	DNA65412-1523	203094	August 4, 1998
	DNA66308-1537	203159	August 25, 1998
	DNA66309-1538	203235	September 15, 1998
	DNA67004-1614	203115	August 11, 1998
50	DNA68869-1610	203164	August 25, 1998
	DNA68872-1620	203160	August 25, 1998
	DNA71159-1617	203135	August 18, 1998

These deposit were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The deposits will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement between Genentech, Inc. and ATCC, which assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC §122 and the Commissioner's rules pursuant thereto (including 37 CFR §1.14 with particular reference to 886 OG 638).

The assignee of the present application has agreed that if a culture of the materials on deposit should die or be lost or destroyed when cultivated under suitable conditions, the materials will be promptly replaced on notification with another of the same. Availability of the deposited material is not to be construed as a license to practice the invention in contravention of the rights granted under the authority of any government in accordance with its patent laws.

The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the construct deposited, since the deposited embodiment is intended as a single illustration of certain aspects of the invention and any constructs that are functionally equivalent are within the scope of this invention. The deposit of material herein does not constitute an admission that the written description herein contained is inadequate to enable the practice of any aspect of the invention, including the best mode thereof, nor is it to be construed as limiting the scope of the claims to the specific illustrations that it represents. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims.

WHAT IS CLAIMED IS:

1. Isolated nucleic acid having at least 80% sequence identity to a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure

284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) and Figure 330 (SEQ ID NO:517).

2. The nucleic acid sequence of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequence selected from the group consisting of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID

NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421), Figure 305 (SEQ ID NO:423), Figure 307 (SEQ ID NO:494), Figure 309 (SEQ ID NO:496), Figure 311 (SEQ ID NO:498), Figure 313 (SEQ ID NO:500), Figure 315 (SEQ ID NO:502), Figure 317 (SEQ ID NO:504), Figure 319 (SEQ ID NO:506), Figure 321 (SEQ ID NO:508), Figure 323 (SEQ ID NO:510), Figure 325 (SEQ ID NO:512), Figure 327 (SEQ ID NO:514) and Figure 329 (SEQ ID NO:516).

3. The nucleic acid of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequence selected from the group consisting of the full-length coding sequence of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure

181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421), Figure 305 (SEQ ID NO:423), Figure 307 (SEQ ID NO:494), Figure 309 (SEQ ID NO:496), Figure 311 (SEQ ID NO:498), Figure 313 (SEQ ID NO:500), Figure 315 (SEQ ID NO:502), Figure 317 (SEQ ID NO:504), Figure 319 (SEQ ID NO:506), Figure 321 (SEQ ID NO:508), Figure 323 (SEQ ID NO:510), Figure 325 (SEQ ID NO:512), Figure 327 (SEQ ID NO:514) and Figure 329 (SEQ ID NO:516).

4. Isolated nucleic acid which comprises the full-length coding sequence of the DNA deposited under any ATCC accession number shown in Table 10.

5. A vector comprising the nucleic acid of Claim 1.

6. The vector of Claim 5 operably linked to control sequences recognized by a host cell transformed with the vector.

7. A host cell comprising the vector of Claim 5.

8. The host cell of Claim 7 wherein said cell is a CHO cell.

9. The host cell of Claim 7 wherein said cell is an *E. coli*.

10. The host cell of Claim 7 wherein said cell is a yeast cell.



11. A process for producing a PRO polypeptides comprising culturing the host cell of Claim 7 under conditions suitable for expression of said PRO polypeptide and recovering said PRO polypeptide from the cell culture.

12. Isolated PRO polypeptide having at least 80% sequence identity to an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID

NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) and Figure 330 (SEQ ID NO:517).

13. Isolated PRO polypeptide having at least 80% sequence identity to the amino acid sequence encoded by a nucleic acid molecule deposited under any ATCC accession number shown in Table 10.

14. A chimeric molecule comprising a polypeptide according to Claim 12 fused to a heterologous amino acid sequence.

15. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is an epitope tag sequence.

16. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is a Fc region of an immunoglobulin.

17. An antibody which specifically binds to a PRO polypeptide according to Claim 12.

18. The antibody of Claim 17 wherein said antibody is a monoclonal antibody.

19. The antibody of Claim 17 wherein said antibody is a humanized antibody.

20. The antibody of Claim 17 wherein said antibody is an antibody fragment.

21. An isolated nucleic acid molecule which has at least 80% sequence identity to a nucleic acid which comprises a nucleotide sequence selected from the group consisting of that shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50

(SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421), Figure 305 (SEQ ID NO:423), Figure 307 (SEQ ID NO:494), Figure 309 (SEQ ID NO:496), Figure 311 (SEQ ID NO:498), Figure 313 (SEQ ID NO:500), Figure 315 (SEQ ID NO:502), Figure 317 (SEQ ID NO:504), Figure 319 (SEQ ID NO:506), Figure 321 (SEQ ID NO:508), Figure 323 (SEQ ID NO:510), Figure 325 (SEQ ID NO:512), Figure 327 (SEQ ID NO:514) and Figure 329 (SEQ ID NO:516).

22. An isolated nucleic acid molecule which has at least 80% sequence identity to the full-length coding sequence of a nucleotide sequence selected from the group consisting of that shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46),  
5 Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure  
10 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID  
15 NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure  
20 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID  
25 NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure  
30 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID  
35 NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure

293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421), Figure 305 (SEQ ID NO:423), Figure 307 (SEQ ID NO:494), Figure 309 (SEQ ID NO:496), Figure 311 (SEQ ID NO:498), Figure 313 (SEQ ID NO:500), Figure 315 (SEQ ID NO:502), Figure 317 (SEQ ID NO:504), Figure 319 (SEQ ID NO:506), Figure 321 (SEQ ID NO:508), Figure 323 (SEQ ID NO:510), Figure 325 (SEQ ID NO:512), Figure 327 (SEQ ID NO:514) and Figure 329 (SEQ ID NO:516).

23. An isolated extracellular domain of of PRO polypeptide.

24. An isolated PRO polypeptide lacking its associated signal peptide.

25. An isolated polypeptide having at least about 80% amino acid sequence identity to an extracellular domain of of PRO polypeptide.

26. An isolated polypeptide having at least about 80% amino acid sequence identity to a PRO polypeptide lacking its associated signal peptide.

27. Isolated nucleic acid having at least 80% nucleic acid sequence identity to:

(a) a nucleotide sequence encoding the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure

169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), lacking its associated signal peptide;

(b) a nucleotide sequence encoding an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID

NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), with its associated signal peptide; or

(c) a nucleotide sequence encoding an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure

90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), lacking its associated signal peptide.

28. An isolated polypeptide having at least 80% amino acid sequence identity to:

(a) the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36),



Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID

NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), lacking its associated signal peptide;

(b) an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID

NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), with its associated signal peptide; or

(c) an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure

254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), lacking its associated signal peptide.

29. A method of detecting a PRO943 polypeptide in a sample suspected of containing a PRO943 polypeptide, said method comprising contacting said sample with a PRO183, PRO184 or PRO185 polypeptide and determining the formation of a PRO943/PRO183, PRO184 or PRO185 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO943 polypeptide in said sample.

30. The method according to Claim 29, wherein said sample comprises cells suspected of expressing said PRO943 polypeptide.

31. The method according to Claim 29, wherein said PRO183, PRO184 or PRO185 polypeptide is labeled with a detectable label.

32. The method according to Claim 29, wherein said PRO183, PRO184 or PRO185 polypeptide is attached to a solid support.

33. A method of detecting a PRO183, PRO184 or PRO185 polypeptide in a sample suspected of containing a PRO183, PRO184 or PRO185 polypeptide, said method comprising contacting said sample with a PRO943 polypeptide and determining the formation of a PRO943/PRO183, PRO184 or PRO185 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO183, PRO184 or PRO185 polypeptide in said sample.

34. The method according to Claim 33, wherein said sample comprises cells suspected of expressing said PRO183, PRO184 or PRO185 polypeptide.

35. The method according to Claim 33, wherein said PRO943 polypeptide is labeled with a detectable label.

36. The method according to Claim 33, wherein said PRO943 polypeptide is attached to a solid support.

37. A method of detecting a PRO331 polypeptide in a sample suspected of containing a PRO331 polypeptide, said method comprising contacting said sample with a PRO1133 polypeptide and determining the formation of a PRO331/PRO1133 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO331 polypeptide in said sample.

38. The method according to Claim 37, wherein said sample comprises cells suspected of expressing said PRO331 polypeptide.

39. The method according to Claim 37, wherein said PRO1133 polypeptide is labeled with a detectable label.

40. The method according to Claim 37, wherein said PRO1133 polypeptide is attached to a solid support.

41. A method of detecting a PRO1133 polypeptide in a sample suspected of containing a PRO1133 polypeptide, said method comprising contacting said sample with a PRO331 polypeptide and determining the formation of a PRO331/PRO1133 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1133 polypeptide in said sample.

42. The method according to Claim 41, wherein said sample comprises cells suspected of expressing said PRO1133 polypeptide.

43. The method according to Claim 41, wherein said PRO331 polypeptide is labeled with a detectable label.

44. The method according to Claim 41, wherein said PRO331 polypeptide is attached to a solid support.

45. A method of detecting a PRO363 or PRO5723 polypeptide in a sample suspected of containing a PRO363 or PRO5723 polypeptide, said method comprising contacting said sample with a PRO1387 polypeptide and determining the formation of a PRO363 or PRO5723/PRO1387 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO363

or PRO5723 polypeptide in said sample.

46. The method according to Claim 45, wherein said sample comprises cells suspected of expressing said PRO363 or PRO5723 polypeptide.

5 47. The method according to Claim 45, wherein said PRO1387 polypeptide is labeled with a detectable label.

48. The method according to Claim 45, wherein said PRO1387 polypeptide is attached to a solid support.

10 49. A method of detecting a PRO1387 polypeptide in a sample suspected of containing a PRO1387 polypeptide, said method comprising contacting said sample with a PRO363 or PRO5723 polypeptide and determining the formation of a PRO363 or PRO5723/PRO1387 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1387 polypeptide in said sample.

15 50. The method according to Claim 49, wherein said sample comprises cells suspected of expressing said PRO1387 polypeptide.

20 51. The method according to Claim 49, wherein said PRO363 or PRO5723 polypeptide is labeled with a detectable label.

52. The method according to Claim 49, wherein said PRO363 or PRO5723 polypeptide is attached to a solid support.

25 53. A method of detecting a PRO1114 polypeptide in a sample suspected of containing a PRO1114 polypeptide, said method comprising contacting said sample with a PRO3301 or PRO9940 polypeptide and determining the formation of a PRO1114/PRO3301 or PRO9940 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1114 polypeptide in said sample.

30 54. The method according to Claim 53, wherein said sample comprises cells suspected of expressing said PRO1114 polypeptide.

35 55. The method according to Claim 53, wherein said PRO3301 or PRO9940 polypeptide is labeled with a detectable label.

56. The method according to Claim 53, wherein said PRO3301 or PRO9940 polypeptide is attached to a solid support.

57. A method of detecting a PRO3301 or PRO9940 polypeptide in a sample suspected of containing a PRO3301 or PRO9940 polypeptide, said method comprising contacting said sample with a PRO1114 polypeptide and determining the formation of a PRO3301 or PRO9940/PRO1114 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO3301 or PRO9940 polypeptide in said sample.

58. The method according to Claim 57, wherein said sample comprises cells suspected of expressing said PRO3301 or PRO9940 polypeptide.

59. The method according to Claim 57, wherein said PRO1114 polypeptide is labeled with a detectable label.

60. The method according to Claim 57, wherein said PRO1114 polypeptide is attached to a solid support.

61. A method of detecting a PRO1181 polypeptide in a sample suspected of containing a PRO1181 polypeptide, said method comprising contacting said sample with a PRO7170, PRO361 or PRO846 polypeptide and determining the formation of a PRO1181/PRO7170, PRO361 or PRO846 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1181 polypeptide in said sample.

62. The method according to Claim 61, wherein said sample comprises cells suspected of expressing said PRO1181 polypeptide.

63. The method according to Claim 61, wherein said PRO7170, PRO361 or PRO846 polypeptide is labeled with a detectable label.

64. The method according to Claim 61, wherein said PRO7170, PRO361 or PRO846 polypeptide is attached to a solid support.

65. A method of detecting a PRO7170, PRO361 or PRO846 polypeptide in a sample suspected of containing a PRO7170, PRO361 or PRO846 polypeptide, said method comprising contacting said sample with a PRO1181 polypeptide and determining the formation of a PRO1181/PRO7170, PRO361 or PRO846 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO7170, PRO361 or PRO846 polypeptide in said sample.

66. The method according to Claim 65, wherein said sample comprises cells suspected of expressing said PRO7170, PRO361 or PRO846 polypeptide.

67. The method according to Claim 65, wherein said PRO1181 polypeptide is labeled with a detectable label.

68. The method according to Claim 65, wherein said PRO1181 polypeptide is attached to a solid support.

69. A method of linking a bioactive molecule to a cell expressing a PRO943 polypeptide, said method comprising contacting said cell with a PRO183, PRO184 or PRO185 polypeptide that is bound to said bioactive molecule and allowing said PRO943 and PRO183, PRO184 or PRO185 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

70. The method according to Claim 69, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

71. The method according to Claim 69, wherein said bioactive molecule causes the death of said cell.

72. A method of linking a bioactive molecule to a cell expressing a PRO183, PRO184 or PRO185 polypeptide, said method comprising contacting said cell with a PRO943 polypeptide that is bound to said bioactive molecule and allowing said PRO943 and PRO183, PRO184 or PRO185 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

73. The method according to Claim 72, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

74. The method according to Claim 73, wherein said bioactive molecule causes the death of said cell.

75. A method of linking a bioactive molecule to a cell expressing a PRO331 polypeptide, said method comprising contacting said cell with a PRO1133 polypeptide that is bound to said bioactive molecule and allowing said PRO331 and PRO1133 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

76. The method according to Claim 75, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.



77. The method according to Claim 75, wherein said bioactive molecule causes the death of said cell.

78. A method of linking a bioactive molecule to a cell expressing a PRO1133 polypeptide, said method comprising contacting said cell with a PRO331 polypeptide that is bound to said bioactive molecule and allowing said PRO331 and PRO1133 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

79. The method according to Claim 78, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

80. The method according to Claim 78, wherein said bioactive molecule causes the death of said cell.

81. A method of linking a bioactive molecule to a cell expressing a PRO1387 polypeptide, said method comprising contacting said cell with a PRO363 or PRO5723 polypeptide that is bound to said bioactive molecule and allowing said PRO1387 and PRO363 or PRO5723 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

82. The method according to Claim 81, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

83. The method according to Claim 81, wherein said bioactive molecule causes the death of said cell.

84. A method of linking a bioactive molecule to a cell expressing a PRO363 or PRO5723 polypeptide, said method comprising contacting said cell with a PRO1387 polypeptide that is bound to said bioactive molecule and allowing said PRO1387 and PRO363 or PRO5723 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

85. The method according to Claim 84, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

86. The method according to Claim 84, wherein said bioactive molecule causes the death of said cell.

87. A method of linking a bioactive molecule to a cell expressing a PRO1114 polypeptide, said method comprising contacting said cell with a PRO3301 or PRO9940 polypeptide that is bound to said bioactive molecule and allowing said PRO1114 and PRO3301 or PRO9940 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

5 88. The method according to Claim 87, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

89. The method according to Claim 87, wherein said bioactive molecule causes the death of said cell.

10 90. A method of linking a bioactive molecule to a cell expressing a PRO3301 or PRO9940 polypeptide, said method comprising contacting said cell with a PRO1114 polypeptide that is bound to said bioactive molecule and allowing said PRO1114 and PRO3301 or PRO9940 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

15 91. The method according to Claim 90, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

20 92. The method according to Claim 90, wherein said bioactive molecule causes the death of said cell.

25 93. A method of linking a bioactive molecule to a cell expressing a PRO1181 polypeptide, said method comprising contacting said cell with a PRO7170, PRO361 or PRO846 polypeptide that is bound to said bioactive molecule and allowing said PRO1181 and PRO7170, PRO361 or PRO846 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

94. The method according to Claim 93, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

30 95. The method according to Claim 93, wherein said bioactive molecule causes the death of said cell.

35 96. A method of linking a bioactive molecule to a cell expressing a PRO7170, PRO361 or PRO846 polypeptide, said method comprising contacting said cell with a PRO1181 polypeptide that is bound to said bioactive molecule and allowing said PRO1181 and PRO7170, PRO361 or PRO846 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

97. The method according to Claim 96, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

98. The method according to Claim 96, wherein said bioactive molecule causes the death of said cell.

99. A method of modulating at least one biological activity of a cell expressing a PRO943 polypeptide, said method comprising contacting said cell with a PRO183, PRO184 or PRO185 polypeptide or an anti-PRO943 antibody, whereby said PRO183, PRO184 or PRO185 polypeptide or said anti-PRO943 antibody binds to said PRO943 polypeptide, thereby modulating at least one biological activity of said cell.

100. The method according to Claim 99, wherein said cell is killed.

101. A method of modulating at least one biological activity of a cell expressing a PRO183, PRO184 or PRO185 polypeptide, said method comprising contacting said cell with a PRO943 polypeptide or an anti-PRO183, anti-PRO184 or anti-PRO185 antibody, whereby said PRO943 polypeptide or said anti-PRO183, anti-PRO184 or anti-PRO185 antibody binds to said PRO183, PRO184 or PRO185 polypeptide, thereby modulating at least one biological activity of said cell.

102. The method according to Claim 101, wherein said cell is killed.

103. A method of modulating at least one biological activity of a cell expressing a PRO331 polypeptide, said method comprising contacting said cell with a PRO1133 polypeptide or an anti-PRO331 antibody, whereby said PRO1133 polypeptide or said anti-PRO331 antibody binds to said PRO331 polypeptide, thereby modulating at least one biological activity of said cell.

104. The method according to Claim 103, wherein said cell is killed.

105. A method of modulating at least one biological activity of a cell expressing a PRO1133 polypeptide, said method comprising contacting said cell with a PRO331 polypeptide or an anti-PRO1133 antibody, whereby said PRO331 polypeptide or said anti-PRO1133 antibody binds to said PRO1133 polypeptide, thereby modulating at least one biological activity of said cell.

106. The method according to Claim 105, wherein said cell is killed.

107. A method of modulating at least one biological activity of a cell expressing a PRO1387 polypeptide, said method comprising contacting said cell with a PRO363 or PRO5723 polypeptide or an anti-PRO1387 antibody, whereby said PRO363 or PRO5723 polypeptide or said anti-PRO1387 antibody binds to said PRO1387 polypeptide, thereby modulating at least one biological activity of said cell.

5 108. The method according to Claim 107, wherein said cell is killed.

109. A method of modulating at least one biological activity of a cell expressing a PRO363 or PRO5723 polypeptide, said method comprising contacting said cell with a PRO1387 polypeptide or an anti-PRO363 or anti-PRO5723 antibody, whereby said PRO1387 polypeptide or said anti-PRO363 or anti-PRO5723  
10 antibody binds to said PRO363 or PRO5723 polypeptide, thereby modulating at least one biological activity of said cell.

110. The method according to Claim 109, wherein said cell is killed.

15 111. A method of modulating at least one biological activity of a cell expressing a PRO1114 polypeptide, said method comprising contacting said cell with a PRO3301 or PRO9940 polypeptide or an anti-PRO1114 antibody, whereby said PRO3301 or PRO9940 polypeptide or said anti-PRO1114 antibody binds to said PRO1114 polypeptide, thereby modulating at least one biological activity of said cell.

20 112. The method according to Claim 111, wherein said cell is killed.

113. A method of modulating at least one biological activity of a cell expressing a PRO3301 or PRO9940 polypeptide, said method comprising contacting said cell with a PRO1114 polypeptide or an anti-PRO3301 or anti-PRO9940 antibody, whereby said PRO1114 polypeptide or said anti-PRO3301 or anti-PRO9940 antibody binds to said PRO3301 or PRO9940 polypeptide, thereby modulating at least one biological  
25 activity of said cell.

114. The method according to Claim 113, wherein said cell is killed.

30 115. A method of modulating at least one biological activity of a cell expressing a PRO1181 polypeptide, said method comprising contacting said cell with a PRO7170, PRO361 or PRO846 polypeptide or an anti-PRO1181 antibody, whereby said PRO7170, PRO361 or PRO846 polypeptide or said anti-PRO1181 antibody binds to said PRO1181 polypeptide, thereby modulating at least one biological activity of said cell.

35 116. The method according to Claim 115, wherein said cell is killed.

117. A method of modulating at least one biological activity of a cell expressing a PRO7170, PRO361 or PRO846 polypeptide, said method comprising contacting said cell with a PRO1181 polypeptide or an anti-PRO7170, anti-PRO361 or anti-PRO846 antibody, whereby said PRO1181 polypeptide or said anti-PRO7170, anti-PRO361 or anti-PRO846 antibody binds to said PRO7170, PRO361 or PRO846 polypeptide, thereby modulating at least one biological activity of said cell.

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118. The method according to Claim 117, wherein said cell is killed.

1/330

**FIGURE 1**

CGGACGCGTGGGTGCGAGGCGAAGGTGACCGGGGACCGAGCATTTTCAGATCTGCTCGGTAGA  
CCTGGTGCACCACCACCATGTTGGCTGCAAGGCTGGTGTGTCTCCGGACACTACCTTCTAGG  
GTTTTCCACCAGCTTTCACCAAGGCCTCCCCTGTTGTGAAGAATTCATCACGAAGAATCA  
ATGGCTGTTAACACCTAGCAGGGAATATGCCACCAAACAAGAATTGGGATCCGGCGTGGGA  
GAACTGGCCAAGAACTCAAAGAGGCAGCATTTGGAACCATCGATGGAAAAAATATTTAAATTT  
GATCAGATGGGAAGATGGTTTGTGTGCTGGAGGGGCTGCTGTTGGTCTTGGAGCATTGTGCTA  
CTATGGCTTGGGACTGTCTAATGAGATTGGAGCTATTGAAAAGGCTGTAATTTGGCCTCAGT  
ATGTCAAGGATAGAATTCATTCCACCTATATGTACTTAGCAGGGAGTATTGGTTTAACAGCT  
TTGTCTGCCATAGCAATCAGCAGAACGCCTGTTCTCATGAACCTCATGATGAGAGGCTCTTG  
GGTGACAATTTGGTGTGACCTTTGCAGCCATGGTTGGAGCTGGAATGCTGGTACGATCAATAC  
CATATGACCAGAGCCCAGGCCCAAAGCATCTTGCTTGGTTGCTACATTCTGGTGTGATGGGT  
GCAGTGGTGGCTCCTCTGACAATATTAGGGGGTCTCTTCTCATCAGAGCTGCATGGTACAC  
AGCTGGCATTTGTGGGAGGCCTCTCCACTGTGGCCATGTGTGCGCCCACTGAAAAGTTTCTGA  
ACATGGGTGCACCCCTGGGAGTGGGCCTGGGTCTCGTCTTTGTGTCTCATTTGGGATCTATG  
TTTCTTCCACCTACCACCGTGGCTGGTGCCACTCTTTACTCAGTGGCAATGTACGGTGGATT  
AGTTCTTTTCAGCATGTTCTTCTGTATGATACCCAGAAAGTAATCAAGCGTGCAGAAGTAT  
CACCAATGTATGGAGTTCAAAAATATGATCCCATTAACCTCGATGCTGAGTATCTACATGGAT  
ACATTAAATATATTTATGCGAGTTGCAACTATGCTGGCAACTGGAGGCAACAGAAAGAATG  
AAGTGACTCAGCTTCTGGCTTCTCTGCTACATCAAATATCTTGTTTAATGGGGCAGATATGC  
ATTAAATAGTTTGTACAAGCAGCTTTCGTTGAAGTTTAGAAGATAAGAAACATGTCATCATA  
TTTAAATGTTCCGGTAATGTGATGCCTCAGGTCTGCCTTTTTTTCTGGAGAATAAATGCAGT  
AATCCTCTCCCAAATAAGCACACACATTTTCAATTCTCATGTTTGAGTGATTTTAAATGTT  
TTGGTGAATGTGAAAATAAGTTTGTGTGTCATGAGAATGTAAGTCTTTTTTCTACTTTAAAA  
TTTAGTAGGTTCACTGAGTAACTAAAATTTAGCAAACCTGTGTTTGCATATTTTTTTGGAGT  
GCAGAATATTGTAATTAATGTCATAAGTGATTTGGAGCTTTGGTAAAGGGACCAGAGAGAAG  
GAGTCACCTGCAGTCTTTTGTTTTTTTAAATACTTAGAACTTAGCACTTGTGTTATTGATTA  
GTGAGGAGCCAGTAAGAAACATCTGGGTATTTGGAAACAAGTGGTCATTGTTACATTCATTT  
GCTGAACCTTAACAAAACCTGTTTCATCCTGAAACAGGCACAGGTGATGCATTCTCCTGCTGTTG  
CTTCTCAGTGCTCTCTTTCCAATATAGATGTGGTCATGTTTGACTTGTACAGAATGTTAATC  
ATACAGAGAATCCTTGATGGAATTATATATGTGTGTTTTACTTTTGAATGTTACAAAAGGAA  
ATAACTTTAAACTATTCTCAAGAGAAAATATTCAAAGCATGAAATATGTTGCTTTTTTCCAG  
AATACAAACAGTATACTCATG

2/330

**FIGURE 2**

MLAARLVCLRTLPSRVFHPAFTKASPVVKNSITKNQWLLTPSREYATKTRIGIRRGRTGQEL  
KEAALEPSMEKIFKIDQMGRWFWAGGAAGVGLGALCYYGGLSNEIGAIEKAVIWPQYVKDRI  
HSTYMYLAGSIGLTALSAIAISRTPVLMNFMMRGSWVTIGVTFAAMVGAGMLVRSIPYDQSP  
GPKHLAWLLHSGVMGAVVAPLTILGGPLLIRAAWYTAGIVGGLSTVAMCAPSEKFLNMGAPL  
GVGLGLVFVSSLGSMFLPPTTVAGATLYSVAMYGGLVLFMFLLYDTQKVIKRAEVSPMYGV  
QKYDPINSMLSIYMDTLNIFMRVATMLATGGRKK

3/330

**FIGURE 3**

GAAGGCTGCCTCGCTGGTCCGAATTCGGTGGCGCCACGTCCGCCCCGTCTCCGCCTTCTGCAT  
CGCGGCTTCGGCGGCTTCCACCTAGACACCTAACAGTCGCGGAGCCGGCCGCGTCGTGAGGG  
GGTCGGCACGGGGAGTCGGGCGGTCTTGTGCATCTTGGCTACCTGTGGGTCTGAAGATGTCGG  
ACATCGGAGACTGGTTTCAGGAGCATCCCGGCGATCACGCGCTATTGGTTCGCGCCACCGTC  
GCCGTGCCCTTGGTCGGCAAACTCGGCCTCATCAGCCGGCCTACCTCTTCCCTCTGGCCCGA  
AGCCTTCCCTTTATCGCTTTTCAGATTTGGAGGGCCAATCACTGCCACCTTTTATTTCCCTGTGG  
GTCCAGGAACCTGGATTTCTTTATTTGGTCAATTTATATTTCTTATATCAGTATTCTACGCGA  
CTTGAAACAGGAGCTTTTGTATGGGAGGCCAGACACTATTTATTCATGCTCCTCTTTAACTG  
GATTTGCATCGTGATTACTGGCTTAGCAATGGATATGCAGTTGCTGATGATTCTCTTGATCA  
TGTCAGTACTTTATGTCTGGGCCCAGCTGAACAGAGACATGATTGTATCATTTTTGGTTTGA  
ACACGATTTAAGGCCTGCTATTTACCCTGGGTTATCCTTGGATTCAACTATATCATCGGAGG  
CTCGGTAATCAATGAGCTTATTGGAAATCTGGTTGGACATCTTTATTTTTTTCCTAATGTTCA  
GATACCCAATGGACTTGGGAGGAAGAAATTTCTATTCACACCTCAGTTTTTGTACCGCTGG  
CTGCCCAGTAGGAGAGGAGGAGTATCAGGATTTGGTGTGCCCCCTGCTAGCATGAGGCGAGC  
TGCTGATCAGAATGGCGGAGGCGGGAGACACAACCTGGGGCCAGGGCTTTCGACTTGGAGACC  
AGTGAAGGGGCGGCCTCGGGCAGCCGCTCCTCTCAAGCCACATTTCTCCCACTGCTGGGTG  
CACTTAACAACCTGCGTTCTGGCTAACACTGTTGGACCTGACCCACACTGAATGTAGTCTTTC  
AGTACGAGACAAAGTTTCTTAAATCCCGAAGAAAAATATAAGTGTTCCACAAGTTTCACGAT  
TCTCATTTCAAGTCCTTACTGCTGTGAAGAACAATAACCAACTGTGCAAATTGCAAAACTGAC  
TACATTTTTTGGTGTCTTCTCTTCTCCCCTTTCCGTCTGAATAATGGGTTTTAGCGGGTCTCT  
AATCTGCTGGCATTGAGCTGGGGCTGGGTACCAAACCCCTTCCCAAAGGACCTTATCTCTT  
TCTTGACACATGCCTCTCTCCCCTTTTCCCAAACCCCACTTTTGCACACTAGAAAAAGTTG  
CCCAATAAATTGCTCTGCCCTTGACAGGTTCTGTTATTTATTGACTTTTGCCAAGGCTGGT  
ACAACAATCATATGTAGCCCTACTGGCTTTTGGTGGCAGAACTGTACCAATAGGGGAG  
AAGACAGCCACGGATGAAGCGTTTCTCAGCTTTTGGAAATGCTTCGACTGACATCCGTTGTT  
AACCGTTTGCCACTCTTCAGATATTTTTTATAAAAAAAGTACCCTGAGTTCATGAGGGCCA  
CAGATTGGTTATTAATGAGATACGAGGGTTGGTGCTGGGTGTTTGTTCCTGAGCTAAGTGA  
TCAAGACTGTAGTGAGTTGCAGCTAACATGGGTTAGGTTTAAACCATGGGGGATGCACCCC  
TTTGCGTTTTCATATGTAGCCCTACTGGCTTTTGGTAGCTGGAGTAGTTGGGTGCTTGTGT  
TAGGAGGATCCAGATCATGTTGGCTACAGGGAGATGCTCTCTTTGAGAGGTCTTGGGCATTG  
ATTCCCATTTCAATCTCATTCTGGATATGTGTTTATTGAGTAAAGGAGGAGAGACCCTCATA  
CGCTATTTAAATGTCACCTTTTTTGCCTATCCCCCGTTTTTTTGGTTCATGTTTCAATTAATTGT  
GAGGAAGGCGCAGCTCCTCTCTGCACGTAGATCATTTTTTTAAAGCTAATGTAAGCACATCTA  
AGGGAATAACATGATTTAAGGTTGAAATGGCTTTTAGAATCATTGTTGGGTTTGAGGGTGTGTTA  
TTTTGAGTCATGAATGTACAAGCTCTGTGAATCAGACCAGCTTAAATACCCACACCTTTTTTT  
TCGTAGGTGGGCTTTTTCTTATCAGAGCTTGGCTCATAACCAAATAAAGTTTTTTTGAAGGCCA  
TGGCTTTTTACACAGTTATTTTTATTTTATGACGTTATCTGAAAGCAGACTGTTAGGAGCAGT  
ATTGAGTGGCTGTCACACTTTGAGGCAACTAAAAAGGCTTCAAACGTTTTGATCAGTTTCTT  
TTCAGGAAACATTTGTGCTCTAACAGTATGACTATTCTTTCCCCCACTCTTAAACAGTGTGAT  
GTGTGTTATCCTAGGAAATGAGAGTTGGCAAACAACCTTCTCATTTTGAATAGAGTTTGTGTG  
TACTTCTCCATATTTAATTTATATGATAAAATAGGTGGGGAGAGTCTGAACCTTAACTGTCA  
TGTTTTGTTGTTTCTGTTGGCCACAATAAAGTTTACTTGTAAAATTTTAGAGGGCCATTACT  
CCAATTATGTTGCACGTACACTCATTGTACAGGCGTGGAGACTCATTGTATGTATAAGAATA  
TTTCTGACAGTGAGTGACCCGGAGTCTCTGGTGTACCCCTTACCAGTCAGCTGCCTGCGAG  
CAGTCATTTTTTCTTAAAGGTTTACAAGTATTTAGAACCTTTTCAGTTCAGGGCAAAATGTTT  
ATGAAGTTATTCCTCTTAAACATGGTTAGGAAGCTGATGACGTTATTGATTTTGTCTGGATT  
ATGTTTCTGGAATAATTTTACCAAAACAAGCTATTTGAGTTTTGACTTGACAAGGCAAAACA  
TGACAGTGGATTCTCTTACAAATGGAATAAATAATCCTTATTTTGTATAAAGGACTTCCC  
TTTTTGTAACATAATCCTTTTTTATTGGTAAAAATTGTAAATTAATAATGTGCAACTTG



4/330

**FIGURE 4**

MSDIGDWFRSIPAITRYWFAATVAVPLVGKLGLISPAYLFLWPEAFLYRFQIWRPITATFYF  
PVGPGTGFLYLVNLYFLYQYSTRLETGAFDGRPADYLFMLLFNWICIVITGLAMDMQLLMIP  
LIMSVLYVWAQLNRDMIVSFWFGTRFKACYLPWVILGFNYIIIGGSVINELIGNLVGHLYFFL  
MFRYPMDLGGRNFLSTPQFLYRWLPSRRGGVSGFGVPPASMRRAADQNGGGGRHNWGQGFRL  
GDQ

**Transmembrane domain:**

amino acids 98-116, 152-172

**N-myristoylation site.**

amino acids 89-95, 168-174, 176-182, 215-221, 221-227, 237-243

**Glycosaminoglycan attachment site.**

amino acids 218-222

5/330

**FIGURE 5**

GGGGCCGCGGTCTAGGGCGGCTACGTGTGTTGCCATAGCGACCATTTTGCATTAACTGGTTG  
GTAGCTTCTATCCTGGGGGCTGAGCGACTGCGGGCCAGCTCTTCCCCTACTCCCTCTCGGCT  
CCTTGTGGCCCAAAGGCCTAACCGGGGTCCGGCGGTCTGGCCTAGGGATCTTCCCCGTTGCC  
CCTTTGGGGCGGG**ATG**GCTGCGGAAGAAGAAGACGAGGTGGAGTGGGTAGTGGAGAGCATCG  
CGGGGTTCTGCGAGGCCAGACTGGTCCATCCCCATCTTGGACTTTGTGGAACAGAAATGT  
GAAGTTAACTGCAAAGGAGGGCATGTGATAACTCCAGGAAGCCCAGAGCCGGTGATTTTGGT  
GGCCTGTGTTCCCCTTGTTTTTGATGATGAAGAAGAAAGCAAATTGACCTATACAGAGATTC  
ATCAGGAATACAAAGAACTAGTTGAAAAGCTGTTAGAAGGTTACCTCAAAGAAATTGGAATT  
AATGAAGATCAATTTCAAGAAGCATGCACTTCTCCTCTTGCAAAGACCCATACATCACAGGC  
CATTTTGAACCTGTGTTGGCAGCAGAAGATTTTACTATCTTTAAAGCAATGATGGTCCAGA  
AAAACATTGAAATGCAGCTGCAAGCCATTGCAATAATTCAAGAGAGAAATGGTGTATTACCT  
GACTGCTTAACCGATGGCTCTGATGTGGTCAGTGACCTTGAACACGAAGAGATGAAAATCCT  
GAGGGAAGTTCTTAGAAAATCAAAAGAGGAATATGACCAGGAAGAAGAAAGGAAGAGGAAAA  
AACAGTTATCAGAGGCTAAAACAGAAGAGCCCACAGTGCATTCCAGTGAAGCTGCAATAATG  
AATAATTCCCAAGGGGATGGTGAACATTTTGCACACCCACCCTCAGAAGTTAAAATGCATTT  
TGCTAATCAGTCAATAGAACCTTTGGGAAGAAAAGTGGAAAGGTCTGAAACTTCCTCCCTCC  
CACAAAAGGCCTGAAGATTCTGGCTTAGAGCATGCGAGCATTGAAGGACCAATAGCAAAC  
TTATCAGTACTTGGAACAGAAGAACTTCGGCAACGAGAACACTATCTCAAGCAGAAGAGAGA  
TAAGTTGATGTCCATGAGAAAGGATATGAGGACTAAACAGATACAAAATATGGAGCAGAAAG  
GAAAACCCACTGGGGAGGTAGAGGAAATGACAGAGAAACCAGAAATGACAGCAGAGGAGAAG  
CAAACATTACTAAAGAGGAGATTGCTTGCAAGAGAACTCAAAGAAGAAGTTATTAATAAG**TA**  
**A**TAATTAAGAACAATTTAACAAAATGGAAGTTCAAATTGTCTTAAAAATAAATTATTTAGTC  
CTTACACTG

6/330

**FIGURE 6**

MAAEEDEVEWVVESIAGFLRGPDWSIPILDFVEQKCEVNCKGGHVITPGSPEPVILVACVP  
LVFDDEEESKLTYTEIHQEYKELVEKLLEGYLKEIGINEDQFQEACTSPLAKTHTSQAILQP  
VLAAEDFTIFKAMMVQKNIEMQLQAIRIIQERNGVLPDCLTDGSDVSDLEHEEMKILREVL  
RKSKEEYDQEEERKRKKQLSEAKTEEPTVHSSEAAIMNNSQGDGEHFAHPPSEVKMHFANQS  
IEPLGRKVERSETSSLPQKGLKIPGLEHASIEGPIANLSVLGTEELRQREHYLKQKRDKLMS  
MRKDMRTKQIQNMEQKGKPTGEVEEMTEKPEMTAEKQTLLKRRLLAEKLKEEVINK

**N-glycosylation sites.**

amino acids 224-228, 246-250, 285-289

**N-myristoylation site.**

amino acids 273-279

**Amidation site.**

amino acids 252-256

**Cytosolic fatty-acid binding proteins.**

amino acids 78-108

7/330

**FIGURE 7**

GGGCACAGCACATGTGAAGTTTTTGATGATGAAGAAGAAAGCAAATTGACCTATACAGAGAT  
TCATCAGGAATACAAAGAAGCTAGTTGAAAAGCTGTTAGAAGGTTACCTCAAAGAAATTGGAA  
TTAATGAAGATCAATTTCAAGAAGCATGCACTTCTCCTCTTGCAAAGACCCATACATCACAG  
GCCATTTTTGCAACCTGTGTTGGCAGCAGAAGATTTTACTATCTTTAAAGCAATGATGGTCC  
AGAAAAACATTGAAATGCAGCTGCAAGCCATTCGAATAATTCAAGAGAGAAATGGTGTATTA  
CCTGACTGCTTAACCGATGGCTCTGATGTGGTCAGTGACCTTGAACACGAAGAGATGAAAAT  
CCTGAGGGAAGTTCTTAGAAAATCAAAAGAGGAATATGACCAGGAA

8/330

**FIGURE 8**

GCGTGGTTTTTGTCTGCAATAGGCGGCTTAGAGGGAGGGGCTTTTTTCGCCTATACCTACTG  
TAGCTTCTCCACGTATGGACCCTAAAGGCTACTGCTGCTACTACGGGGCTAGACAGTTACTG  
TCTCAGCTCTAGGATGTGCGTTCTTCCACTAGAAGCTCTTCTGAGGGAGGTAATTA AAAAAC  
AGTGGAA**ATG**GAAAAACAGTGCTGTAGTCATCCTGTAATATGCTCCTTGTCAACAATGTATAC  
ATTCTGCTAGGTGCCATATTCATTGCTTTAAGCTCAAGTCGCATCTTACTAGTGAAGTATT  
CTGCCAATGAAGAAAACAAGTATGATTATCTTCCAACCTACTGTGAATGTGTGCTCAGAACTG  
GTGAAGCTAGTTTTCTGTGTGCTTGTGTCAATCTGTGTTATAAAGAAAGATCATCAAAGTAG  
AAATTTGAAATATGCTTCCTGGAAGGAATTCTCTGATTTTCATGAAGTGGTCCATTCTGCCT  
TTCTTTATTTTCTGGATAACTTGATTGTCTTCTATGTCTGTCTATCTTCAACCAGCCATG  
GCTGTTATCTTCTCAAATTTTAGCATTATAACAACAGCTCTTCTATTCAAGGATAGTGCTGAA  
GAGGCGTCTAAACTGGATCCAGTGGGCTTCCCTCCTGACTTTATTTTTTGTCTATTGTGGCCT  
TGACTGCCGGGACTAAACTTTACAGCACAACTTGGCAGGACGTGGATTTTCATCACGATGCC  
TTTTTTCAGCCCTTCCAATTCCTGCCTTCTTTTCAGAAGTGAGTGTCCAGAAAAGACAATTG  
TACAGCAAAGGAATGGACTTTTCTGAAGCTAAATGGAACACCACAGCCAGAGTTTTTCAGTC  
ACATCCGTCTTGGCATGGGCCATGTTCTTATTATAGTCCAGTGTTTTATTTCTTCAATGGCT  
AATATCTATAATGAAAAGATACTGAAGGAGGGGAACCAGCTCACTGAAAGCATCTTCATACA  
GAACAGCAAACCTCTATTTCTTTGGCATTCTGTTTAATGGGCTGACTCTGGGCCTTCAGAGGA  
GTAACCGTGATCAGATTAAGAACTGTGGATTTTTTTTATGGCCACAGTGCATTTTTCAGTAGCC  
CTTATTTTTTGTAACTGCATTCCAGGGCCTTTCAGTGGCTTTCATTCTGAAGTTCCTGGATAA  
CATGTTCCATGTCTTGATGGCCCAGGTTACCACTGTCAATTATCACAAACAGTGTCTGTCTCTGG  
TCTTTGACTTCAGGCCCTCCCTGGAATTTTTCTTGAAGCCCCATCAGTCCTTCTCTCTATA  
TTTATTTTATAATGCCAGCAAGCCTCAAGTTCGGGAATACGCACCTAGGCAAGAAAGGATCCG  
AGATCTAAGTGGCAATCTTTGGGAGCGTTCCAGTGGGGATGGAGAAGAACTAGAAAGACTTA  
CCAAACCCAAGAGTGATGAGTCAGATGAAGATACTTTC**TAA**CTGGTACCCACATAGTTTTGCA  
GCTCTCTTGAACCTTATTTTTCACATTTTTCAGTGTTTGTAATATTTATCTTTTCACTTTGATA  
AACCAGAAATGTTTCTAAATCCTAATATTCTTTGCATATATCTAGCTACTCCCTAAATGGTT  
CCATCCAAGGCTTAGAGTACCCAAAGGCTAAGAAATTCTAAAGAACTGATACAGGAGTAACA  
ATATGAAGAATTCATTAATATCTCAGTACTTGATAAATCAGAAAGTTATATGTGCAGATTAT  
TTTCCTTGGCCTTCAAGCTTCCAAAAAACTTGTAATAATCATGTTAGCTATAGCTTGTATAT  
ACACATAGAGATCAATTTGCCAAATATTACAAATCATGTAGTTCTAGTTTACATGCCAAAGT  
CTTCCCTTTTTTAACATTATAAAAGCTAGGTTGTCTCTTGAATTTTGAGGCCCTAGAGATAGT  
CATTTTGCAAGTAAAGAGCAACGGGACCCTTCTAAAAACGTTGGTTGAAGGACCTAAATAC  
CTGGCCATACCATAGATTTGGGATGATGTAGTCTGTGCTAAATATTTTGCTGAAGAAGCAGT  
TTCTCAGACACAACATCTCAGAATTTTAATTTTTTAGAAATTCATGGGAAATTGGATTTTTGT  
AATAATCTTTTGATGTTTTTAACATTGGTTCCCTAGTCACCATAGTTACCACTTGTATTTTA  
AGTCATTTTAAACAAGCCACGGTGGGGCTTTTTTCTCCTCAGTTTGAGGAGAAAAATCTTGAT  
GTCATTACTCCTGAATTATTACATTTTGGAGAATAAGAGGGCATTTTATTTTATTAGTTACT  
AATTCAAGCTGTGACTATTGTATATCTTTCCAAGAGTTGAAATGCTGGCTTCAGAATCATAC  
CAGATTGTCAGTGAAGCTGATGCCTAGGAACTTTTAAAGGGATCCTTTCAAAGGATCACTT  
AGCAAACACATGTTGACTTTTAACTGATGTATGAATATTAATACTCTAAAAATAGAAAGACC  
AGTAATATATAAGTCACCTTACAGTGCTACTTCACACTTAAAGTGCATGGTATTTTTTCATG  
GTATTTTGCATGCAGCCAGTTAACTCTCGTAGATAGAGAAGTCAGGTGATAGATGATATTAA  
AAATTAGCAAACAAAAGTGACTTGCTCAGGGTCATGCAGCTGGGTGATGATAGAAGAGTGGG  
CTTTAACTGGCAGGCCTGTATGTTTACAGACTACCATACTGTAAATATGAGCTTTATGGTGT  
CATTCTCAGAACTTATACATTTCTGCTCTCCTTTCTCCTAAGTTTCATGCAGATGAATATA  
AGGTAATATACTATTATATAATTCATTTGTGATATCCACAATAATATGACTGGCAAGAATTG  
GTGGAAATTTGTAATTAAATAATTATTAAACCT

9/330

**FIGURE 9**

MEKQCCSHPVICSLSTMYTFLLGAIFIALSSSRILLVKYSANEENKYDYLPTTVNVCSELVK  
LVFCVLVSFCVIKKDHQSRNLKYASWKEFSDFMKWSIPAFLYFLDNLIVFYVLSYLQPAMAV  
IFS NFSIITTALLFRIVLKRRLNWIQWASLLTLFLSIVALTAGTKTLQHNLAGRGFHHDAFF  
SPSNSCLLFRSECPRKDNCTAKEWTFPEAKWNTTARVFSHIRLGMGHVLIIVQCFISSMANI  
YNEKILKEGNQLTESIFIQNSKLYFFGILFNGLTLGLQRSNRDQIKNCGFFYGHS AFSVALI  
FVTAFQGLSVAFILKFLDNMFHVLMAQVTTVIIITTVSVLVFDFRPSLEFFLEAPSVLLSIFI  
YNASKPQVPEYAPRQERIRDL SGNLWERSSSGDGEELERLTKPKSDESD EDTF

**Transmembrane domains:**

amino acids 16-36 (type II), 50-74, 147-168, 229-250, 271-293,  
298-318, 328-368

**N-glycosylation sites.**

amino acids 128-132, 204-208, 218-222, 374-378

**Glycosaminoglycan attachment site.**

amino acids 402-406

**N-myristoylation sites.**

amino acids 257-263, 275-281, 280-286, 284-290, 317-323

10/330

**FIGURE 10**

CGTGCCTGCGCAATGGGTGTCGGGTCCGCTTTTTCCCAATCCGGACGTAATCGTGGTTTTTG  
TTCTGCAATAGGCGGCTTAGAGGGAGGGGCTTTTTCGCCTATACCTACTGTAGCTTCTCCAC  
GTATGGACCCCTAAAGGCTACTGCTGCTACTACGGGGCTAGACAGTTACTGTCTCAGCTCTAG  
GATGTGCGTTCTTCCACTAGAAGCTCTTCTGAGGGAGGTAATTAAAAACAGTGGAATGGAA  
AAACAGTGCTGTAGTCATCCTGTAATATGCTCCTTGTCAACAATGTATACATTCCCTGCTAGG  
TGCCATATTCATTGCTTTAAGCTCAAGTCGCATCTTACTAGTGAAGTATTCTGCCAATGAAG  
AAAACAAGTATGATTATCTTCCAACACTGTGAATGTGTGCTCAGAACTGGTGAAGCTAGTT  
TTCTGTGTGCTTGTGTCATTCTGTGTTATAAAGAAAGATCATCAAAGTAGAAATTTGAAATA  
TGCTTCCTGGAAGGAATTCTCTGATTTTCATGAAGTGGTCCATTCCCTGCCTTTCTTTATTTCC  
TGGATAACTTGATTGTCTTCTATGTCCTGTCCTATCTTCAACCAGCCATGGCTGTTATCTTC  
TCAAATTTTAGCATTATAACAACAGCTCTTCTATTTCAGGATAGTGCTGAAGAGGCGTCTAAA  
CTGGATCCAGTGGGCTTCCCTCCTGACTTTATTTTTGTCTATTGTGGCCTTGACTGCCGGGA  
CTAAACTTTA

11/330

**FIGURE 11**

CGGACGCGTGGGCGGACGCGTGGGCGGACGCGTGGGGCCGGCTTGGCTAGCGCGCGGGCGGCC  
GTGGCTAAGGCTGCTACGAAGCGAGCTTGGGAGGAGCAGCGGCCTGCGGGGCAGAGGAGCAT  
CCCGTCTACCAGGTCCCAAGCGGCGTGGCCCGCGGGTCATGGCCAAAGGAGAAGGCGCCGAG  
AGCGGCTCCGCGGGCGGGGCTGCTACCCACCAGCATCCTCCAAAGCACTGAACGCCCGGCCCA  
GGTGAAGAAAGAACCAGAAAAAGAAACAACAGTTGTCTGTTTGCAACAAGCTTTGCTATG  
CACTTGGGGGAGCCCCCTACCAGGTGACGGGCTGTGCCCTGGGTTTCTTCCCTTCAGATCTAC  
CTATTGG**ATG**TGGCTCAGGTGGGCCCTTTCTCTGCCTCCATCATCCTGTTTGTGGGCCGAGC  
CTGGGATGCCATCACAGACCCCCTGGTGGGCCTCTGCATCAGCAAATCCCCCTGGACCTGCC  
TGGGTGCCTTATGCCCTGGATCATCTTCTCCACGCCCCTGGCCGTCATTGCCTACTTCCTC  
ATCTGGTTCGTGCCCCGACTTCCCACACGGCCAGACCTATTGGTACCTGCTTTTCTATTGCCT  
CTTTGAAACAATGGTCACGTGTTTCCATGTTCCCTACTCGGCTCTCACCATGTTTCATCAGCA  
ACCGAGCAGACTGAGCGGGATTCTGCCACCGCCTATCGGATGACTGTGGAAGTGCTGGGCAC  
AGTGCTGGGCACGGCGATCCAGGGACAAATCGTGGGCCAAGCAGACACGCCTTGTTTCCAGG  
ACTTCAATAGCTCTACAGTAGCTTCACAAAGTGCCAACCATAACATGGCACCACCTTCACAC  
AGGGAAACGCAAAGGCATACCTGCTGGCAGCGGGGGTCAATTGTCTGTATCTATATAATCTG  
TGCTGTCATCCTGATCCTGGGCGTGCGGGAGCAGAGAGAACCCTATGAAGCCCAGCAGTCTG  
AGCCAATCGCCTACTTCCGGGGCCTACGGCTGGTCATGAGCCACGGCCCATAACATCAAACCT  
ATTACTGGCTTCCTCTTCACCTCCTTGGCTTTTCATGCTGGTGGAGGGGAACCTTTGTCTTGT  
TTGCACCTACACCTTGGGCTTCCGCAATGAATTCCAGAATCTACTCCTGGCCATCATGCTCT  
CGGCCACTTTAACCATTCCCATCTGGCAGTGGTTCTTGACCCGGTTTGGAAGAAGACAGCT  
GTATATGTTGGGATCTCATCAGCAGTGCCATTTCTCATCTTGGTGGCCCTCATGGAGAGTAA  
CCTCATCATTACATATGCGGTAGCTGTGGCAGCTGGCATCAGTGTGGCAGCTGCCTTCTTAC  
TACCCTGGTCCATGCTGCCTGATGTCATTGACGACTTCCATCTGAAGCAGCCCCACTTCCAT  
GGAACCGAGCCCATCTTCTTCTCCTTCTATGTCTTCTTCACCAAGTTTGCCTCTGGAGTGTC  
ACTGGGCATTTCTACCCTCAGTCTGGACTTTGCAGGGTACCAGACCCGTGGCTGCTCGCAGC  
CGGAACGTGTCAAGTTTACACTGAACATGCTCGTGACCATGGCTCCCATAGTTCTCATCCTG  
CTGGGCCTGCTGCTCTTCAAATGTACCCCATTTGATGAGGAGAGGCGGCGGCAGAATAAGAA  
GGCCCTGCAGGCACTGAGGGACGAGGCCAGCAGCTCTGGCTGCTCAGAAACAGACTCCACAG  
AGCTGGCTAGCATCCTC**TAG**GGCCCGCCACGTTGCCCGAAGCCACCATGCAGAAGGCCACAG  
AAGGGATCAGGACCTGTCTGCCGGCTTGCTGAGCAGCTGGACTGCAGGTGCTAGGAAGGGAA  
CTGAAGACTCAAGGAGGTGGCCAGGACACTTGCTGTGCTCACTGTGGGGCCGGCTGCTCTG  
TGGCCTCCTGCCTCCCCTCTGCCTGCCTGTGGGGCCAAGCCCTGGGGCTGCCACTGTGAATA  
TGCCAAGGACTGATCGGGCCTAGCCCGGAACACTAATGTAGAAACCTTTTTTTTACAGAGCC  
TAATTAATAACTTAATGACTGTGTACATAGCAATGTGTGTGTATGTATATGTCTGTGAGCTA  
TTAATGTTATTAATTTTCATAAAAGCTGGAAAGC



12/330

**FIGURE 12**

MWLRWALSLPPSSCLWAEPGMPSQTPWWASASANPPGPAWVALCPGSSSPRPWPSLPTSSSG  
SCPTSHTARPIGTCFSIASLKQWSRVSMFPTRLSPCSSATEQTERDSATAYRMTVEVLGTVL  
GTAIQQQIVGQADTPCFQDFNSSTVASQSANHHTGTTSHRETQKAYLLAAGVIVCIYIICAV  
ILILGVREQREPYEAQQSEPIAYFRGLRLVM SHGPYIKLITGFLFTSLAFMLVEGNFVLFCT  
YTLGFRNEFQNLLLAIMLSATLTIPIWQWFLTRFGKKTAVYVGISSAVPFLILVALMESNLI  
ITYAVAVAAGISVAAAFLLPWSMLPDVIDDFHLKQPHFHGTEPIFFSFYVFFTKFASGVSLG  
ISTLSLDFAGYQTRGCSQPERVKFTLNMLVTMAPIVLILLGLLLFKMYPIDEERRRQNKAL  
QALRDEASSSGCSETDSTELASIL

13/330

**FIGURE 13**

GGGAAACGCAAAAGGCATACCTGCTGGCAGCGGGGGTCATTGTCTGTATCTATATAATCTGT  
GCTGTCATCCTGATCCTGGGCGTGCGGGAGCAGAGAGAACCCTATGAAGCCCAGCAGTCTGA  
GCCAATCGCCTACTTCCGGGGCCTACGGCTGGTCATGAGCCACGGCCCATACATCAAACCTTA  
TTACTGGCTTCCTCTTCACCTCCTTGGCTTTCATGCTGGTGGAGGGGAACTTTGTCTTGTTT  
TGCACCTACACCTTGGGCTTCCGCAATGAATTCCAGAATCTACTCCTGGCCATCATGCTCTC  
GGCCACTTTAACCATTCCCATCTGGCAGTGGTTCTTGACCCGGTTTGGCAAGAAGACAGCTG  
TATATGTTGGGATCTCATCAGCAGTGCCATTTCTCATCTTGGTGGCCCTCATGGAGAGTAAC  
CTCATCATTACATATGCGGTAGCTGTGGCAGCTGGCATCAGTGTGGCAGCTGCCTTCTTACT  
ACCCTGGTCCATGCTGCCTGATGTCATTGACGACTTCCATCTGAAGCAGCCCCACTTCCATG  
GAACCGAGCCCAT

14/330

**FIGURE 14**

GGGGCTTCGGCGCCAGCGGCCAGCGCTAGTCGGTCTGGTAAGGATTTACAAAAGGTGCAGGT  
ATGAGCAGGTCTGAAGACTAACATTTTGTGAAGTTGTAAAACAGAAAACCTGTTAGAA**ATGT**  
GGTGGTTTCAGCAAGGCCTCAGTTTCCTTCCTTCAGCCCTTGTAATTTGGACATCTGCTGCT  
TTCATATTTTCATACATTACTGCAGTAACACTCCACCATATAGACCCGGCTTTACCTTATAT  
CAGTGACACTGGTACAGTAGCTCCAGAAAAATGCTTATTTGGGGCAATGCTAAATATTGCGG  
CAGTTTTATGCATTGCTACCATTTATGTTTCGTTATAAGCAAGTTCATGCTCTGAGTCCTGAA  
GAGAACGTTATCATCAAATTAAACAAGGCTGGCCTTGTAAGTCTGGAATACTGAGTTGTTTAGG  
ACTTTCTATTGTGGCAAACCTTCAGAAAAACAACCCTTTTTGCTGCACATGTAAGTGGAGCTG  
TGCTTACCTTTGGTATGGGCTCATTATATATGTTTGTTCAGACCATCCTTTTCTACCAAATG  
CAGCCCCAAAATCCATGGCAAACAAGTCTTCTGGATCAGACTGTTGTTGGTTATCTGGTGTGG  
AGTAAGTGCACCTTAGCATGCTGACTTGCTCATCAGTTTTGCACAGTGGCAATTTTGGGACTG  
ATTTAGAACAGAACTCCATTGGAACCCCGAGGACAAAGGTTATGTGCTTCACATGATCACT  
ACTGCAGCAGAAATGGTCTATGTCATTTTCCTTCTTTGGTTTTTTTCTGACTTACATTCGTGA  
TTTTCAGAAAATTTCTTTACGGGTGGAAGCCAATTTACATGGATTAACCCTCTATGACACTG  
CACCTTGCCCTATTAACAATGAACGAACACGGCTACTTTCCAGAGATATTT**TGAT**GAAAGGAT  
AAAATATTTCTGTAATGATTATGATTCTCAGGGATTGGGGAAAGGTTACAGAAAGTTGCTTA  
TTCTTCTCTGAAATTTTCAACCACTTAATCAAGGCTGACAGTAACACTGATGAATGCTGATA  
ATCAGGAAACATGAAAGAAGCCATTTGATAGATTATTCTAAAGGATATCATCAAGAAGACTA  
TTAAAAACACCTATGCCTATACTTTTTTATCTCAGAAAATAAAGTCAAAAGACTATG

15/330

**FIGURE 15**

MWWFQQGLSFLPSALVIWTSAAFIIFSYYITAVTLHHIDPALPYISDTGTVAPEKCLFGAMLNI  
AAVLCIATIIYVRYKQVHALSPEENVIIKLNKAGLVLGILSCLGLSIVANFQKTTLFAAHVSG  
AVLTFGMGSLYMFVQTILSYQMOPKIHGKQVFWIRLLLVIWCGVSALSMLTCSSVLHSGNFG  
TDLEQKLHWNPEDKGYVLHMITTAAEWSMSFSFFGFLTYIRDFQKISLRVEANLHGLTLYD  
TAPCPINNERTRLLSRDI

16/330

**FIGURE 16**

CGGACGCTTGGGCNGCGCCAGCGGCCAGCGCTAGTCGGTCTGGTAAGTGCCTGATGCCGAGT  
TCCGTCTCTCGGGTCTTTTCCTGGTCCCAGGCAAAGCGGAGCGGAGATCCTCAAACGGCCTA  
GTGCTTCGCGCTTCCGGAGAAAATCAGCGGTCTAATTAATTCCTCTGGTTTGTTGAAGCAGT  
TACCAAGAATCTTCAACCCTTTCCCACAAAAGCTAATTGAGTACACGTTCTGTTGAGTACA  
CGTTCCTGTTGATTTACAAAAGGTGCAGGTATGAGCAGGTCTGAAGACTAACATTTTGTGAA  
GTTGTAAAACAGAAAACCTGTTAGAAATGTGGTGGTTTCAGCAAGGCCTCAGTTTCCTTCCT  
TCAGCCCTTGTAATTTGGACATCTGCTGCTTTCATATTTTCATACATTACTGCAGTAACACT  
CCACCATATAGACCCGGCTTTACCTTATATCAGTGACACTGGTACAGTANC

17/330

**FIGURE 17**

CCCACGCGTCCGCCCCGCGCTGCGTCCCGGAGTGCAAGTGAGCTTCTCGGCTGCCCCGCGGG  
CCGGGGTGCGGAGCCGAC**ATG**CGCCCCGCTTCTCGGCCTCCTTCTGGTCTTCGCCGGCTGCAC  
CTTCGCCTTGTACTTGCTGTGACGCGACTGCCCCGCGGGCGGAGACTGGGCTCCACCGAGG  
AGGCTGGAGGCAGGTCGCTGTGGTTCCCCCTCCGACCTGGCAGAGCTGCGGGAGCTCTCTGAG  
GTCCTTCGAGAGTACCGGAAGGAGCACCAGGCCTACGTGTTCCCTGCTCTTCTGCGGCGCCTA  
CCTCTACAAACAGGGCTTTGCCATCCCCGGCTCCAGCTTCCTGAATGTTTTAGCTGGTGCCT  
TGTTTGGGCCATGGCTGGGGCTTCTGCTGTGCTGTGTGTGACCTCGGTGGGTGCCACATGC  
TGCTACCTGCTCTCCAGTATTTTTGGCAAACAGTTGGTGGTGTCTACTTTCCTGATAAAGT  
GGCCCTGCTGCAGAGAAAGGTGGAGGAGAACAGAAACAGCTTGTTTTTTTTTCTTATTGTTTT  
TGAGACTTTTCCCCATGACACCAAACCTGGTTCTTGAACCTCTCGGCCCCAATTCTGAACATT  
CCCATCGTGCAGTTCTTCTTCTCAGTTCTTATCGGTTTGATCCCATATAATTCATCTGTGT  
GCAGACAGGGTCCATCCTGTCAACCCTAACCTCTCTGGATGCTCTTTTCTCCTGGGACACTG  
TCTTTAAGCTGTTGGCCATTGCCATGGTGGCATTAATTCCTGGAACCCTCATTAAAAAATTT  
AGTCAGAAACATCTGCAATTGAATGAAACAAGTACTGCTAATCATATACACAGTAGAAAAGA  
CACAT**TGA**TCTGGATTTTCTGTTTGCCACATCCCTGGACTCAGTTGCTTATTTGTGTAATGGA  
TGTGGTCCTCTAAAGCCCCTCATTGTTTTTGATTGCCTTCTATAGGTGATGTGGACACTGTG  
CATCAATGTGCAGTGTCTTTTCAGAAAGGACACTCTGCTCTTGAAGGTGTATTACATCAGGT  
TTTCAAACCAGCCCTGGTGTAGCAGACACTGCAACAGATGCCTCCTAGAAAATGCTGTTTGT  
GGCCGGGCGCGGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCCGGTGATTC  
ACAAGGTCAGGAGTTCAAGACCAGCCTGGCCAAGATGGTGAAATCCTGTCTCTAATAAAAAT  
ACAAAAATTAGCCAGGCGTGGTGGCAGGCACCTGTAATCCCAGCTACTCGGGAGGCTGAGGC  
AGGAGAATTGCTTGAACCAAGGTGGCAGAGGTTGCAGTAAGCCAAGATCACACCACTGCACT  
CCAGCCTGGGTGATAGAGTGAGACACTGTCTTGAC

18/330

**FIGURE 18**

MRPLLGLLLVFAGCTFALYLLSTRLPGRRLGSTEEAGGRSLWFPSDLAELRELVREYR  
KEHQAYVFLLFCGAYLYKQGFaipGSSFLNVLAGALFGPWLGLLLCCVLTsvgATCCYLLSS  
IFGKQLVVSYPDPKVALLQRKVEENRNSLFFFLFLRLFPMTPNWFLNLSAPILNIPIVQFF  
FSVLIGLIPYNFICVQTGSILSTLTSLDALFSWDTVFKLLAIAMVALIPGTLIKKFSQKHLQ  
LNETSTANHIHSRKDT

**Important features:****Signal peptide:**

amino acids 1-17

**Transmembrane domains:**

amino acids 101-123, 189-211

**N-glycosylation sites.**

amino acids 172-176, 250-254

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 240-244, 261-265

**N-myristoylation site.**

amino acids 13-19, 104-110, 115-121, 204-210

**Amidation site.**

amino acids 27-31

**Prokaryotic membrane lipoprotein lipid attachment site.**

amino acids 4-15

**Protein splicing proteins.**

amino acids 25-31

**Sugar transport proteins.**

amino acids 162-172

19/330

**FIGURE 19**

CCGAGGCGGGAGGAGCCCCGAGGGGGCGCGAGCCCCGCATGAATCATTGTAGTCAATCATTTT  
CCAGTTCTCAGCCGCTCAGTTGTGATCAAGGGACACGTGGTTTCCGAACTGCCAGCTCAGAA  
TAGGAAAATAACTTGGGATTTTATATTGGAAGAC**ATG**GATCTTGCTGCCAACGAGATCAGCA  
TTTATGACAAACTTTCAGAGACTGTTGATTTGGTGAGACAGACCGGCCATCAGTGTGGCATG  
TCAGAGAAGGCAATTGAAAAATTTATCAGACAGCTGCTGGAAAAGAATGAACCTCAGAGACC  
CCCCCGCAGTATCCTCTCCTTATAGTTGTGTATAAGGTTCTCGCAACCTTGGGATTAATCT  
TGCTCACTGCCTACTTTGTGATTCAACCTTTCAGCCCATTAGCACCTGAGCCAGTGCTTTCT  
GGAGCTCACACCTGGCGCTCACTCATCCATCACATTAGGCTGATGTCCTTGCCCATTGCCAA  
GAAGTACATGTCAGAAAATAAGGGAGTTCCTCTGCATGGGGGTGATGAAGACAGACCCTTTC  
CAGACTTTGACCCCTGGTGGACAAACGACTGTGAGCAGAATGAGTCAGAGCCCATTCTGCC  
AACTGCACTGGCTGTGCCCAGAAACACCTGAAGGTGATGCTCCTGGAAGACGCCCCAAGGAA  
ATTTGAGAGGCTCCATCCACTGGTGATCAAGACGGGAAAGCCCCTGTTGGAGGAAGAGATTC  
AGCATTTTTTGTGCCAGTACCCTGAGGCGACAGAAGGCTTCTCTGAAGGGTTTTTCGCCAAG  
TGGTGGCGCTGCTTTCCTGAGCGGTGGTTCCCATTTCCTTATCCATGGAGGAGACCTCTGAA  
CAGATCACAAATGTTACGTGAGCTTTTTCTGTCTTCACTCACCTGCCATTTCCAAAAGATG  
CCTCTTTAAACAAGTGCTCCTTTCCTCACCCAGAACCTGTTGTGGGGAGTAAGATGCATAAG  
ATGCCTGACCTATTTATCATTGGCAGCGGTGAGGCCATGTTGCAGCTCATCCCTCCCTTCCA  
GTGCCGAAGACATTGTCAGTCTGTGGCCATGCCAATAGAGCCAGGGGATATCGGCTATGTCTG  
ACACCACCCACTGGAAGGTCTACGTTATAGCCAGAGGGGTCCAGCCTTTGGTCATCTGCGAT  
GGAACCGCTTTCTCAGAACTG**TAG**GAAATAGAACTGTGCACAGGAACAGCTTCCAGAGCCGA  
AAACCAGGTTGAAAGGGGAAAAATAAAAACAAAACGATGAAACTGCAAAAA



20/330

**FIGURE 20**

MDLAANEISIIYDKLSETVDLVRQTGHQCGMSEKAIEKFIRQLLEKNEPQRPPPQYPLLIVVY  
KVLATLGLILLTAYFVIQPFSPLAPEPVLGAHTWRSLIHHIRLMSLPPIAKKYMSENKGVPL  
HGGDEDRPFPDFDPWWTNDCEQNESEPI PANCTGCAQKHLKVMLLEDAPRKFERLHPLVIKT  
GKPLLEEEIQHFLCQYPEATEGFSEGFFAKWWRCFPERWFPPYPWRRPLNRSQMLRELFV  
FTHLPFPKDASLNKCSFLHPEPVVGSKMHKMPDLFIIGSGEAMLQLIPPFQCRRHCSVAMP  
IEPGDIGYVDTTHWKVYVIARGVQPLVICDGTAFSEL

21/330

**FIGURE 21**

CCACGGTGTCCGTTCTTCGCCCCGGCGGCAGCTGTCCCCGAGGCGGGAGGAGCCCCGAGGGGCG  
CGAGCCCCGCATGAATCATTGTAGTCAATCATTTTCCAGTTCTCAGCCGTTTCAGTTGTGATC  
AAGGGACACGTGGTTTCCGAACTGCCAGCTCAGAATAGGAAAATAACTTGGGATTTTATATT  
GGAAGACATGGATCTTGCTGCCAACGAGATCAGCATTTATGACAACTTTCAGAGACTGTTG  
ATTTGGTGAGACAGACCGGCCATCAGTGTGGCATGTCAGAGAAGGCAATTGAAAAATTTATC  
AGACAGCTGCTGGAAAAGAATGAACCTCAGAGACCCCCCCCCGCAGTATCCTCTCCTTATAGT  
TGTGTATAAGGTTCTCGCAACCTTGGGATTAATCTTGCTCACTGCCTACTTTGTGATTCAAC  
CTTTCAGCCCATTAGCACCTGAGCCAGTGCTTTGTGGAGCTCAC

22/330

**FIGURE 22**

CCCACGCGTCCGCCCACGCGTCCGGCTGAACACCTCTTCTTTGGAGTCAGCCACTGATGAGG  
CAGGGTCCCCACTTGCAGCTGCAGCAGCTGCAGCAGCTGCAGAGCGCTGCTCCTGGCTGGTG  
CCACTGGTGCGCACGCTGCTAGACCGTGCCTATGAGCCGCTGGGGCTGCAGTGGGGACTGCC  
CTCCCTGCCACCCACCAATGGCAGCCCCACCTTCTTTGAAGACTTCCAGGCTTTTTGTGCCA  
CACCCGAATGGCGCCACTTCATCGACAAACAGGTACAGCCAACC**ATG**TCCAGTTCGAAATG  
GACACGTATGCTAAGAGCCACGACCTTATGTCAGGTTTCTGGAATGCCTGCTATGACATGCT  
TATGAGCAGTGGGCAGCGGCCAGTGGGAGCGCGCCAGAGTCGTCGGGCCCTTCCAGGAGC  
TGGTGCTGGAACCTGCGCAGAGGGCGGGCGCCTGGAGGGGCTACGCTACACGGCAGTGTG  
AAGCAGCAGGCAACGCAGCACTCCATGGCCCTGCTGCAGTGGGGGGCGCTGTGGCGCCAGCT  
CGCCAGCCCATGTGGGGCCTGGGCGCTGAGGGACACTCCCATCCCCCGCTGGAAACTGTCCA  
GCGCCGAGACATATTACGCATGCGTCTGAAGCTGGTGCCCAACCATCACTTCGACCCTCAC  
CTGGAAGCCAGCGCTCTCCGAGACAATCTGGGTGAGGTTCCCCTGACACCCACCGAGGAGGC  
CTCACTGCCTCTGGCAGTGACCAAAGAGGCCAAAGTGAGCACCCACCCAGTGTGCTGCAGG  
AGGACCAGCTCGGCGAGGACGAGCTGGCTGAGCTGGAGACCCCGATGGAGGCAGCAGAACTG  
GATGAGCAGCGTGAGAAGCTGGTGCTGTGCGCCGAGTGCCAGCTGGTGACGGTAGTGGCCGT  
GGTCCCAGGGCTGCTGGAGGTCACCACACAGAATGTATACTTCTACGATGGCAGCACTGAGC  
GCGTGGAACCCGAGGAGGGCATCGGCTATGATTTCCGGCGCCCACTGGCCAGCTGCGTGAG  
GTCCACCTGCGGCGTTTCAACCTGCGCGCTTACGACCTTGAAGCTTCTTCTTATCGATCAGGC  
CAACTACTTCCCTCAACTTCCCATGCAAGGTGGGCACGACCCAGTCTCATCTCCTAGCCAGA  
CTCCGAGACCCAGCCTGGCCCCATCCCACCCCATACCCAGGTACGGAACCAGGTGTACTCG  
TGGCTCCTGCGCCTACGGCCCCCTCTCAAGGCTACCTAAGCAGCCGCTCCCCCAGGAGAT  
GCTGCGTGCCTCAGGCCTTACCCAGAAATGGGTACAGCGTGAGATATCCAACTTCGAGTACT  
TGATGCAACTCAACACCATTTGCGGGGCGGACCTACAATGACCTGTCTCAGTACCCTGTGTTC  
CCCTGGGTCCCTGCAGGACTACGTGTCCCCAACCCCTGGACCTCAGCAACCCAGCCGTCTTCCG  
GGACCTGTCTAAGCCCATCGGTGTGGTGAACCCCAAGCATGCCAGCTCGTGAGGGAGAAGT  
ATGAAAGCTTTGAGGACCCAGCAGGGACCATTGACAAGTTCCACTATGGCACCCACTACTCC  
AATGCAGCAGGCGTGATGCACTACCTCATCCGCGTGGAGCCCTTCACCTCCCTGCACGTCCA  
GCTGCAAAGTGGCCGCTTTGACTGCTCCGACCGGCAGTTCCTCAGTGGCGGCAGCCCTGGC  
AGGCACGCTGGAGAGCCCTGCCGATGTGAAGGAGCTCATCCCGGAATTCTTCTACTTTCTCT  
GACTTCCTGGAGAACCAGAACGGTTTTGACCTGGGCTGTCTCCAGCTGACCAACGAGAAGGT  
AGGCGATGTGGTGCTACCCCCGTGGGCCAGCTCTCCTGAGGACTTCATCCAGCAGCACC GCC  
AGGCTCTGGAGTCGGAGTATGTGTCTGCACACCTACACGAGTGGATCGACCTCATCTTTGGC  
TACAAGCAGCGGGGGCCAGCCGCGGAGGAGCCCTCAATGTCTTCTATTACTGCACCTATGA  
GGGGGCTGTAGACTGGACCATGTGACAGATGAGCGGGAACGGAAGGCTCTGGAGGGCATTA  
TCAGCAACTTTGGGCAGACTCCCTGTGAGCTGCTGAAGGAGCCACATCCAACTCGGCTCTCA  
GCTGAGGAAGCAGCCCATCGCCTTGCACGCCTGGACACTAACTCACCTAGCATCTTCCAGCA  
CCTGGACGAACTCAAGGCATTCTTCGCAGAGGTGACTGTGAGTGCCAGTGGGCTGCTGGGCA  
CCCACAGCTGGTTGCCCTATGACCGCAACATAAGCAACTACTTCAGCTTCAGCAAAGACCCC  
ACCATGGGCAGCCACAAGACGCAGCGACTGCTGAGTGGCCCGTGGGTGCCAGGCAGTGGTGT  
GAGTGGACAAGCACTGGCAGTGGCCCCGGATGGAAAGCTGCTATTACGCGGTGGCCACTGGG  
ATGGCAGCCTGCGGGTGACTGCACTACCCCGTGGCAAGCTGTTGAGCCAGCTCAGCTGCCAC  
CTTGATGTAGTAACCTGCCTTGCAGTGGACACCTGTGGCATCTACCTCATCTCAGGCTCCCG  
GGACACCACGTGCATGGTGTGGCGGCTCCTGCATCAGGGTGGTCTGTGCTAGTAGGCCTGGCAC  
CAAAGCCTGTGCAGGTCTGTATGGGCATGGGGCTGCAGTGAGCTGTGTGGCCATCAGCACT  
GAACTTGACATGGCTGTGTCTGGATCTGAGGATGGAAGTGTGATCATAACACTGTACGCCG  
CGGACAGTTTGTAGCGGCACTACGGCCTCTGGGTGCCACATTCCCTGGACCTATTTTCCACC  
TGGCATTGGGGTCCGAAGGCCAGATTGTGGTACAGAGCTCAGCGTGGGAACGTCTGGGGCC  
CAGGTACCTACTCCTTGCACCTGTATTCACTCAATGGGAAGTTGCGGGCTTCACTGCCCT  
GGCAGAGCAGCCTACAGCCCTGACGGTGACAGAGGACTTTGTGTTGTGTTGGGACCCGCCAGT  
GCGCCCTGCACATCCTCCAACATAACACACTGCTCCCGGCCGCGCCTCCCTTGCCCATGAAG  
GTGGCCATCCGCAGCGTGGCCGTGACCAAGGAGCGCAGCCACGTGCTGGTGGGCCCTGGAGGA  
TGGCAAGCTCATCGTGGTGGTTCGCGGGGCGAGCCCTCTGAGGTGCGCAGCAGCCAGTTCGCGC  
GGAAGCTGTGGCGGTCTCGCGGCGCATCTCCAGGTGTCCTCGGGAGAGACGGAATAACAAC  
CCTACTGAGCGCGCT**TGA**ACTGGCCAGTCCCGGCTGCTCGGGCCCCCGCCCGCAGCCCTG  
GCCCCGGGAGGGCCCCGCCAGAAGTCGGCGGGGAACACCCCGGGTGGGCAGCCAGGGGGTGA  
GCGGGGCCCCACCTGCCCAGCTCAGGGATTGGCGGGCGATGTTACCCCTCAGGGATTGGCG  
GGCGGAAGTCCCGCCCCCTCGCCGGCTGAGGGGCCGCCCTGAGGGCCAGCACTGGCGTCT

23/330

**FIGURE 23**

MSQFEMDTYAKSHDLMSGFWNACYDMLMSSGQRRQWERAQSRRAFQELVLEPAQRRARLEGL  
RYTAVLKQQATQHSMALLHWGALWRQLASPCGAWALRDTPIPRWKLSSAETYSRMRLKLVPN  
HHFDPHLEASALRDNLGEVPLTPTEEASLPLAVTKEAKVSTPPELLQEDQLGEDELALETP  
MEAAELDEQREKLVLSAECQLVTVVAVVPGLLEVTTQNVYFYDGSTERVETE EGIGYDFRRP  
LAQLREVHLRRFNLRRSALELFFIDQANYFLNFPCKVGTTPVSSPSQTPRPQPGPIPPHTQV  
RNQVYSWLLRLRPSSQGYLSSRSPQEMLRASGLTQKWVQREISNFEYLMQLNTIAGR TYNDL  
SQYPVFPWVLQDYVSPTLDLSNPAVFRDLSPKIGVVNPKHAQLVREKYESFEDPAGTIDKFH  
YGTHYSNAAGVMHYLIRVEPFTSLHVQLQSGRFDCSDRQFHSVAAAWQARLESPADV KELIP  
EFFYFPDFLENQNGFDLGCLQLTNEKVGDVVLPWPASSPEDFIQQHRQALESEYVSAHLHEW  
IDLIFGYKQRGPAEEALNVFYCYTEGAVDLDHVTDERERKALEGIISNFGQTPCQLLKEP  
HPTRLSAEEAAHRLARLDTNSPSIFQHLDELKAFFAEVTVSASGLLGTHSWLPYDRNISNYF  
SFSKDPTMGSHKTQRLLSGPWVPGSGVSGQALAVAPDGKLLFSGGHWGSLRVTALPRGKLL  
SQLSCHLDVVTCLALDTCGIY LISGSRDTTCMVWRL LHQGGLSVGLAPKPVQVLYGHGA AVS  
CVAISTELDMAVSGSEDGTVIIHTVRRGQFVAALRPLGATFPGPIFHLALGSEGQIVVQSSA  
WERPGAQVTYSLHLYSVNGKLRLASLPLAEQPTALTVTEDFVLLGTAQCALHILQLNTLLPAA  
PPLPMKVAIRSVAVTKERSHVLVGLLEDGKLIVVVAGQPSEVRSSQFARKLWRSSRRISQVSS  
GETEYNPTEAR

**N-glycosylation site.**

amino acids 677-681

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 985-989

**Tyrosine kinase phosphorylation site.**

amino acids 56-65, 367-376, 543-551

**N-myristoylation site.**amino acids 61-67, 436-442, 604-610, 610-616, 664-670, 691-697,  
706-712, 711-717, 769-775, 785-791, 802-808, 820-826, 834-840,  
873-879, 912-918, 954-960

24/330

**FIGURE 24**

**CGG**ACGCGTGGGCGGACGCGTGGGGGCTGTGAGAAAGTGCCAATAAATACATCATGCAACCC  
CACGGCCCACCTTGTGAACTCCTCGTGCCCAGGGCTGATGTGCGTCTTCCAGGGCTACTCAT  
CCAAAGGCCTAATCCAACGTTCTGTCTTCAATCTGCAAATCTATGGGGTCTTGGGGCTCTTC  
TGGACCCTTAACTGGGTACTGGCCCTGGGCCAATGCGTCCTCGCTGGAGCCTTTGCCTCCTT  
CTACTGGGCCTTCCACAAGCCCCAGGACATCCCTACCTTCCCCTTAATCTCTGCCTTCATCC  
GCACACTCCGTTACCACACTGGGTCATTGGCATTGAGGCCCTCATCCTGACCCTTGTGCAG  
ATAGCCCGGGTCATCTTGGAGTATATTGACCACAAGCTCAGAGGAGTGCAGAACCCTGTAGC  
CCGCTGCATCATGTGCTGTTTCAAGTGCTGCCTCTGGTGTCTGGAAAAATTTATCAAGTTCC  
TAAACCGCAATGCATACATCATGATCGCCATCTACGGGAAGAATTTCTGTGTCTCAGCCAAA  
AATGCGTTCATGCTACTCATGCGAAACATTGTCAGGGTGGTCGTCCTGGACAAAGTCACAGA  
CCTGCTGCTGTTCTTTGGGAAGCTGCTGGTGGTCGGAGGCGTGGGGGTCCTGTCTTCTTTT  
TTTTCTCCGGTCGCATCCCGGGGCTGGGTAAAGACTTTAAGAGCCCCCACCTCAACTATTAC  
TGGCTGCCCATCATGACCTCCATCCTGGGGGCCTATGTCATCGCCAGCGGCTTCTTCAGCGT  
TTTCGGCATGTGTGTGGACACGCTCTTCCTCTGCTTCCTGGAAGACCTGGAGCGGAACAACG  
GCTCCCTGGACCGGCCCTACTACATGTCCAAGAGCCTTCTAAAGATTCTGGGCAAGAAGAAC  
GAGGCGCCCCCGGACAACAAGAAGAGGAAGAAG**TGA**CAGCTCCGGCCCTGATCCAGGACTGC  
ACCCACCCCCACCGTCCAGCCATCCAACCTCACTTCGCCTTACAGGTCTCCATTTTGTGGT  
AAAAAAGGTTTTAGGCCAGGCGCCGTGGCTCACGCCTGTAATCCAACACTTTGAGAGGCTG  
AGGCGGGCGGATCACCTGAGTCAGGAGTTCGAGACCAGCCTGGCCAACATGGTGAAACCTCC  
GTCTCTATTAAAAATACAAAAATTAGCCGAGAGTGGTGGCATGCACCTGTCATCCCAGCTAC  
TCGGGAGGCTGAGGCAGGAGAATCGCTTGAACCCGGGAGGCAGAGGTGTCAGTGAGCCGAGA  
TCGCGCCACTGCACTCCAACCTGGGTGACAGACTCTGTCTCCAAAACAAAACAAACAAACAA  
AAAGATTTTATTAAAGATATTTTGTTAACCTC

25/330

**FIGURE 25**

RTRGRTRGGCEKVPINTSCNPTAHLVNSSCPGLMCVFQGYSSKGLIQRSVFNLQIYGVLGLF  
WTLNWVLALGQCVLAGAFASFYWAFHKPQDIPTFPLISAFIRTLRYHTGSLAFGALILTLVQ  
IARVILEYIDHKLRGVQNPVARCIMCCFKCCLWCLEKFIKFLNRNAYIMIAIYGKNFCVSAK  
NAFMLLMRNIVRVVLDKVTDLLFFGKLLVGGVGVLSFFFFSGRIPGLGKDFKSPHLNYY  
WLPIMTSILGAYVIASGFFSVFGMCVDTLFLCFLEDLERNNGSLDRPYMSKSLLKILGKN  
EAPPDNKKRKK

26/330

**FIGURE 26**

GAGTCTTGACCGCCGCCGGGCTCTTGGTACCTCAGCGCGAGCGCCAGGCGTCCGGCCGCCGT  
GGCT**ATG**TTCGTGTCCGATTTCCGCAAAGAGTTCTACGAGGTGGTCCAGAGCCAGAGGGTCC  
TTCTCTTCGTGGCCTCGGACGTGGATGCTCTGTGTGCGTGCAAGATCCTTCAGGCCTTGTTTC  
CAGTGTGACCACGTGCAATATACGCTGGTTCCAGTTTCTGGGTGGCAAGAACTTGAAACTGC  
ATTTCTTGAGCATAAAGAACAGTTTCATTATTTTATTCTCATAAACTGTGGAGCTAATGTAG  
ACCTATTGGATATTCTTCAACCTGATGAAGACACTATATTCTTTGTGTGTGACTCCCATAGG  
CCAGTCAATGTCGTCAATGTATACAACGATACCCAGATCAAATTACTCATTAACAAGATGA  
TGACCTTGAAGTTCCCGCCTATGAAGACATCTTCAGGGATGAAGAGGAGGATGAAGAGCATT  
CAGGAAATGACAGTGATGGGTGAGAGCCTTCTGAGAAGCGCACACGGTTAGAAGAGGAGATA  
GTGGAGCAAACCATGCGGAGGAGGCAGCGGCGAGAGTGGGAGGCCCGGAGAAGAGACATCCT  
CTTTGACTACGAGCAGTATGAATATCATGGGACATCGTCAGCCATGGTGATGTTTGAGCTGG  
CTTGATGCTGTCCAAGGACCTGAATGACATGCTGTGGTGGGCCATCGTTGGACTAACAGAC  
CAGTGGGTGCAAGACAAGATCACTCAAATGAAATACGTGACTGATGTTGGTGTCTTGCAGCG  
CCACGTTTCCCGCCACAACCACCGGAACGAGGATGAGGAGAACACACTCTCCGTGGACTGCA  
CACGGATCTCCTTTGAGTATGACCTCCGCCTGGTGCTCTACCAGCACTGGTCCCTCCATGAC  
AGCCTGTGCAACACCAGCTATACCGCAGCCAGGTTCAAGCTGTGGTCTGTGCATGGACAGAA  
GCGGCTCCAGGAGTTCCTTGACAGACATGGGTCTTCCCCTGAAGCAGGTGAAGCAGAAGTTCC  
AGGCCATGGACATCTCCTTGAAGGAGAATTTGCGGGAAATGATTGAAGAGTCTGCAAATAAA  
TTTGGGATGAAGGACATGCGCGTGACAGACTTTCAGCATTCAATTTGGGTTCAGGCACAAGTT  
TCTGGCCAGCGACGTGGTCTTTGCCACCATGTCTTTGATGGAGAGCCCCGAGAAGGATGGCT  
CAGGGACAGATCACTTCATCCAGGCTCTGGACAGCCTCTCCAGGAGTAACCTGGACAAGCTG  
TACCATGGCCTGGAACCTCGCCAAGAGCAGCTGCGAGCCACCCAGCAGACCATTGCCAGCTGC  
CTTTGCACCAACCTCGTCATCTCCAGGGGCCTTTCTGTACTGCTCTCTCATGGAGGGCAC  
TCCAGATGTCATGCTGTTCTCTAGGCCGGCATCCCTAAGCCTGCTCAGCAAACACCTGCTCA  
AGTCCTTTGTGTGTTTCGACAAAGAACCGGCGCTGCAAACCTGCTGCCCTGGTGATGGCTGCC  
CCCCTGAGCATGGAGCATGGCACAGTGACCGTGGTGGGCATCCCCCAGAGACCGACAGCTC  
GGACAGGAAGAACTTTTTTGGGAGGGCGTTTGAGAAGGCAGCGGAAAGCACCAGCTCCCGGA  
TGCTGCACAACCATTTTGACCTCTCAGTAATTGAGCTGAAAGCTGAGGATCGGAGCAAGTTT  
CTGGACGCACTTATTTCCCTCCTGTCC**TAG**GAATTTGATTCTTCCAGAATGACCTTCTTATT  
TATGTAACCTGGCTTTCATTTAGATTGTAAGTTATGGACATGATTTGAGATGTAGAAGCCATT  
TTTTATTAAATAAAATGCTTATTTTAGGAAA

27/330

**FIGURE 27**

MFVSDFRKEFYEVVQSQRVLLFVASDVDALCACKILQALFQCDHVQYTLVPVSGWQELETAF  
LEHKEQFHYFILINCGANVDLLDILQPDEDTIFFVCDSHRPVNVVNVYNDTQIKLLIKQDDD  
LEVPAIEDIFRDEEEDDEEHSGNDSGSEPSEKRTRLEEEIVEQTMRRRQRREWEARRRDILF  
DYEQYEHGTSSAMVMFELAWMLSKDLNDMLWWAIVGLTDQWVQDKITQMKYVTDVGVLQRH  
VSRHNHRNEDEENTLSVDCTRISFEYDLRLVLYQHWSLHDSL CNTSYTAARFKLWSVHGQKR  
LQEF LADMGLPLKQVKQKFQAMD ISLKENLREMIEESANKFGMKDMRVQTF SIHFGFKHKFL  
ASDVVFATMSLMESPEKDGSGTDHFIQALDSLRSNLDKLYHGLELAKKQLRATQQTIASCL  
CTNLVISQGPFLYCSLMEGTPDVMLFSRPASLSLLSKHLLKSFVCSTKNRRCKLLPLVMAAP  
LSMEHGTVTTVVGIPPETDSSDRKNFFGRAFEKAAESTSSRMLHNFHFDLSVIELKAEDRSKFL  
DALISLLS



28/330

**FIGURE 28**

GTACCTCAGCGCGAGCGCCAGGCGTCCGGCCGCCGTGGCTATGNTCGTGTCCGATTTCCGCA  
AAGAGTTCTACGAGGTGGTCCAGAGCCAGAGGGTCCTTCTCTTCGTGGCCTCGGANGTGGAT  
GCTCTGTGTGCGTGCAAGATCCTTCAGGCCTTGTTCCAGTGTGACCANGTGCAATATANGCT  
GGTTCCAGTTTCTGGGTGGCAAGAACTTGAACTGCATTTCTTGAGCATAAAGAACAGTTTC  
ATTATTTTATTCTCATAACTGTGGAGCTAATGTAGACCTATTGGATATTCTTCAACCTGAT  
GAAGACACTATATTCTTTGTGTGTGACACCCATAGGCCAGTCAATGTTGTCAATGTATACAA  
CGATACCC

29/330

**FIGURE 29**

CAGGAACCCTCTCTTTGGGTCTGGATTGGGACCCCTTTCCAGTACCATTTTTTCTAGTGAAC  
CACGAAGGGACGATACCAGAAAAACACCCTCAACCCAAAGGAAATAGACTACAGCCCCAATTG  
GCTGACTTTTGGCTATAGAAAAAGAAAGGAACGAAAAGAGACAGTTTTTTTTGGAAAGCTAA  
GTCTTCCCTTTATCGAGTCAAGAAACCCCCCTTCTTGAGCTATTTACAGCTTTTAAACAATT  
GAGTAAAGTACGCTCCGGTCACCA**ATG**GTGACAGCCGCCCTGGGTCCCGTCTGGGCAGCGCTC  
CTGCTCTTTCTCCTGATGTGTGAGATCCGTATGGTGGAGCTCACCTTTGACAGAGCTGTGGC  
CAGCGGCTGCCAACGGTGCTGTGACTCTGAGGACCCCTGGATCCTGCCCATGTATCCTCAG  
CCTCTTCCCTCCGGCCGCCCCACGCCCTGCCTGAGATCAGACCCTACATTAATATCACCATC  
CTGAAGGGTGACAAAGGGGACCCAGGCCCAATGGGCCTGCCAGGGTACATGGGCAGGGAGGG  
TCCCCAAGGGGAGCCTGGCCCTCAGGGCAGCAAGGGTGACAAGGGGGAGATGGGCAGCCCCG  
GCGCCCCGTGCCAGAAGCGCTTCTTCGCCTTCTCAGTGGGCCGCAAGACGGCCCTGCACAGC  
GGCGAGGACTTCCAGACGCTGCTCTTCGAAAGGGTCTTTGTGAACCTTGATGGGTGCTTTGA  
CATGGCGACCGGCCAGTTTGCTGCTCCCTGCGTGGCATCTACTTCTTACGCCTCAATGTGC  
ACAGCTGGAATTACAAGGAGACGTACGTGCACATTATGCATAACCAGAAAGAGGCTGTCATC  
CTGTACGCGCAGCCCAGCGAGCGCAGCATCATGCAGAGCCAGAGTGTGATGCTGGACCTGGC  
CTACGGGGACCGCGTCTGGGTGCGGCTCTTCAAGCGCCAGCGCGAGAACGCCATCTACAGCA  
ACGACTTCGACACCTACATCACCTTCAGCGGCCACCTCATCAAGGCCGAGGACGAC**TGA**GGG  
CCTCTGGGCCACCCTGCCGGCTGGAGAGCTCAGGTGCTGGTCCCGTCCCTGCAGGGCTCAG  
TTTGCACTGCTGTGAAGCAGGAAGGCCAGGGAGGTCCCCGGGGACCTGGCATTTCTGGGGAGA  
CCCTGCTTCTATCTTGGCTGCCATCATCCCTCCCAGCCTATTTCTGCTCCTCTCTTCTCTCT  
TGGACCTATTTTAAAGAAGCTTGCTAACCTAAATATTCTAGAACTTTCCCAGCCTCGTAGCCC  
AGCACTTCTCAAACCTTGGAATGCATGCGAATCACCCGGGGTTCGTGTTAAATGCAGATTCT  
GACTCAGCAGGTCTGAGTGGGTCCAGGATTCTGTGTTTCTCATATGTTCCCTGGGTGATGCTG  
ATGGGGTCAGTCTATGAACCACACTGGAGCAACCAGGTTCTAGGACTTCTCAATATTCTAG  
TACTTTCTGAACATTCTGGAATCCTCCCCACATTCTAGAATTCTCCCAACATTTTTTTTTTCT  
TGAGACAGAGTCTTGCTCTGTTGCCCAGGCTAGAGTGCAGTGGTGCAATCTCAGTTCAGTGC  
AACCTCTGCCTCCCGGGTTCGAAGCGATTCTTCTGCCTCAGCCTCCCTAGTGGCTGGGATTAC  
AGGCGCCTGCTACCATGCCTGGCTAATTTTTGTATTTTTAGTAGAGATGGGGTTTACCATA  
TTGGCCAGGCTGGTCTTGAACCTCTGACTTCAGGTGACCCACCCGCCTCGGCCTCTCAAAAT  
GCTGGGATTACAGGTGTGAGCCACCGTGCCTGGCCAATTCCAACATTCTTAAATTCTCTCAT  
CCCTCCAGGGCTCCCCGTGCTATGTTCTCTTTACCCCTTCCCCCTCTTCTCTTGCTCAGGCC  
TGCACCACTGCAGCCACCGTTCATTTTATTCAATTCATTAAACACTGAGCACTCACTCTGTGCT  
GGGTCCCGGGAAGGGTGAGGGGGTCAAGACACAGGCCCTGCCCTGCCCTCAGTGAAGTGGCCA  
GTCCAGCCCAGGCGGGGAGAGATGTGTACATAGGTTTTAAAGCAGACCCAGAGCTCATGGGG  
GCCTGTGTTCTGGGTGTTCAAGGTGCTGCTGGTCCCTCCATTACCCACTGCTCCCCAAGGCTGG  
TGGGACGGGGTCCCGGTGGCAGGGGGCAGGTATCTCCTTCCCGTTCCTCATCCACCTGCCAG  
TGCTCATCGTTACAGCAAACCCCAGGGGGCCTTGGCCAGGTCAAGGGTCTGTGAGGAGAGG  
ACCCAGGAGTGTGGGGGCATTTGGGGGGTGAAGTGGCCCCCGAAGAATGGAACCCACACCCA  
TAGCTCTCCCCACAGCTGATACGGCATCCTGCGAGAAGACCTGCCCTCCTCACTGGGATCCC  
CTTCTGCTCCTCCCAGGGCTCTGCCAGGGCCTTGCTCAGTCCCTTCCACCAAAGTCATCT  
GAACTTCCGTTTCCCCAGGGCCTCCAGCTGCCCTCAGACACTGATGTCTGTCCCCAGGTGCT  
CTCTGCCCTCATGCCCTCTCACCGGCCAGTGCCCCGACTCTCCAGGCTTTATCAAGGTG  
CTAAGGCCCGGGTGGGCAGTCTCGTCTCAGAGCCCTCCTCCGGCCTGGTGCTGCCTTTAC  
AAACACCTGCAGGAGAAGGGCCACGGAAGCCCCAGGCTTTAGAGCCCTCAGCAGGTCTGGGG  
AGCTAGAGCAAAGGAGGGACCTCAGGCCTTCCGTTTTCTTCTTCCAGGGTGGGGTGGCCTGGT  
GTTCCCTAGCCTTCCAAACCCAGGTGGCCTGCCCTTCTCCCCAGAGGGAGGCGGCCTCCGC  
CCATTGGTGCTCATGCAGACTCTGGGGCTGAGGTGCCCGGGGGGTGATCTCTGGTGCTCAC  
AGCCGAGGGAGCCGTGGCTCCATGGCCAGATGACGGAACAGGGTCTGACCAAGTGCCAGGA  
AGACCTGTGCTATAAACACCCTGCCTGATCTGCCCTGCCTGACCCCGCCACGCCCTGCC  
GTCCAGCATGATTAAAGAATGCTGTCTCCTCTTGGAATAAAAAAAAAAAAAA

30/330

**FIGURE 30**

MVTAALGPVWAALLLFLLMCEIRMVELTFDRAVASGCQRCCDSEDPLDPAHVSSASSSGRPH  
ALPEIRPYINITILKGDKGDPGPMGLPGYMGREGPGQGEPPQGSKGDKGEMGSPGAPCQKRF  
FAFSVGRKTALHSGEDFQTLLFERVFVNLDGCFDMATGQFAAPLRGIYFFSLNVHSWNYKET  
YVHIMHNQKEAVILYAQPSESRIMQSQSVMLDLAYGDRVWVRLFKRQRENAIYSNDFDTYIT  
FSGHLIKAEDD

**Important features:****Signal peptide:**

amino acids 1-20

**N-glycosylation site.**

amino acids 72-75

**Clq domain proteins.**

amino acids 144-178, 78-111 and 84-117

31/330

**FIGURE 31**

ACTCGAACGCAGTTGCTTCGGGACCCAGGACCCCCCTCGGGCCCGACCCGCCAGGAAAGACTG  
AGGCCGCGGCCTGCCCCGCCCCGGCTCCCTGCGCCGCCGCCGCTCCCGGGACAGAAG**ATGTG**  
CTCCAGGGTCCCTCTGCTGCTGCCGCTGCTCCTGCTACTGGCCCTGGGGCCTGGGGTGCAGG  
GCTGCCCATCCGGCTGCCAGTGCAGCCAGCCACAGACAGTCTTCTGCACTGCCCGCCAGGGG  
ACCACGGTGCCCCGAGACGTGCCACCCGACACGGTGGGGCTGTACGTCTTTGAGAACGGCAT  
CACCATGCTCGACGCAGGCAGCTTTGCCGGCCTGCCGGGCCTGCAGCTCCTGGACCTGTCAC  
AGAACCAGATCGCCAGCCTGCCAGCGGGGTCTTCCAGCCACTCGCCAACCTCAGCAACCTG  
GACCTGACGGCCAACAGGCTGCATGAAATCACCAATGAGACCTTCCGTGGCCTGCGGCGCCT  
CGAGCGCCTCTACCTGGGCAAGAACCGCATCCGCCACATCCAGCCTGGTGCCTTCGACACGC  
TCGACCGCCTCCTGGAGCTCAAGCTGCAGGACAACGAGCTGCGGGCACTGCCCCCGCTGCGC  
CTGCCCCGCTGCTGCTGCTGGACCTCAGCCACAACAGCCTCCTGGCCCTGGAGCCCGGCAT  
CCTGGACACTGCCAACGTGGAGGCGCTGCGGCTGGCTGGTCTGGGGCTGCAGCAGCTGGACG  
AGGGGCTCTTCAGCCGCTTGCGCAACCTCCACGACCTGGATGTGTCCGACAACCAGCTGGAG  
CGAGTGCCACCTGTGATCCGAGGCCTCCGGGGCCTGACGCGCCTGCGGCTGGCCGGCAACAC  
CCGCATTGCCAGCTGCGGCCCCGAGGACCTGGCCGGCCTGGCTGCCCTGCAGGAGCTGGATG  
TGAGCAACCTAAGCCTGCAGGCCCTGCCTGGCGACCTCTCGGGCCTCTTCCCCCGCCTGCGG  
CTGCTGGCAGCTGCCCGCAACCCCTTCAACTGCGTGTGCCCCCTGAGCTGGTTTGGCCCTG  
GGTGC GCGAGAGCCACGTCACACTGGCCAGCCCTGAGGAGACGCGCTGCCACTTCCCGCCCA  
AGAACGCTGGCCGGCTGCTCCTGGAGCTTGACTACGCCGACTTTGGCTGCCAGCCACCACC  
ACCACAGCCACAGTGCCCAACCACGAGGCCCGTGGTGCGGGAGCCACAGCCTTGTCTTCTAG  
CTTGGCTCCTACCTGGCTTAGCCCCACAGCGCCGGCCACTGAGGCCCCCAGCCCGCCCTCCA  
CTGCCCCACCGACTGTAGGGCCTGTCCCCCAGCCCCAGGACTGCCACCGTCCACCTGCCTC  
AATGGGGGCACATGCCACCTGGGGACACGGCACCACTGGCGTGCTTGTGCCCCGAAGGCTT  
CACGGGCCTGTACTGTGAGAGCCAGATGGGGCAGGGGACACGGCCCAGCCCTACACCAGTCA  
CGCCGAGGCCACCACGGTCCCTGACCCTGGGCATCGAGCCGGTGAGCCCCACCTCCCTGCGC  
GTGGGGCTGCAGCGCTACCTCCAGGGGAGCTCCGTGCAGCTCAGGAGCCTCCGTCTCACCTA  
TCGCAACCTATCGGGCCCTGATAAGCGGCTGGTGACGCTGCGACTGCCTGCCTCGCTCGCTG  
AGTACACGGTCACCCAGCTGCGGCCCCAACGCCACTTACTCCGTCTGTGTATGCCTTTGGGG  
CCCCGGGCGGGTGCCGGAGGGCGAGGAGGCCTGCGGGGAGGGCCATACACCCCCAGCCGTCCA  
CTCCAACCACGCCCCAGTCACCCAGGCCCGCGAGGGCAACCTGCCGCTCCTCATTGCGCCCG  
CCCTGGCCGCGGTGCTCCTGGCCGCGCTGGCTGCGGTGGGGGCAGCCTACTGTGTGCGGCGG  
GGGCGGGCCATGGCAGCAGCGGCTCAGGACAAAGGGCAGGTGGGGCCAGGGGCTGGGCCCT  
GGAAGTGGAGGGAGTGAAGGTCCCCTTGAGGCCAGGCCCGAAGGCAACAGAGGGCGGTGGAG  
AGGCCCTGCCAGCGGGTCTGAGTGTGAGGTGCCACTCATGGGCTTCCCAGGGCCTGGCCTC  
CAGTCACCCCTCCACGCAAAGCCCTACATC**TAA**GCCAGAGAGAGACAGGGCAGCTGGGGCCG  
GGCTCTCAGCCAGTGAGATGGCCAGCCCCCTCCTGCTGCCACACCACGTAAGTTCTCAGTCC  
CAACCTCGGGGATGTGTGCAGACAGGGCTGTGTGACCACAGCTGGGCCCTGTTCCCTCTGGA  
CCTCGGTCTCCTCATCTGTGAGATGCTGTGGCCAGCTGACGAGCCCTAACGTCCCCAGAAC  
CGAGTGCCCTATGAGGACAGTGTCCGCCCTGCCCTCCGCAACGTGCAGTCCCTGGGCACGGCG  
GGCCCTGCCATGTGCTGGTAACGCATGCCTGGGTCTGCTGGGCTCTCCCACTCCAGGCGGA  
CCCTGGGGGCCAGTGAAGGAAGCTCCCGGAAAGAGCAGAGGGAGAGCGGGTAGGCGGCTGTG  
TGACTCTAGTCTTGGCCCCAGGAAGCGAAGGAACAAAAGAACTGGAAAGGAAGATGCTTTA  
GGAACATGTTTTGCTTTTTTAAAATATATATATTTATAAGAGATCCTTTCCCATTTATTCTG  
GGAAGATGTTTTTCAAACCTCAGAGACAAGGACTTTGGTTTTTGTAAAGACAAACGATGATATG  
AAGGCCTTTTGTAAAGAAAAAATAAAAGATGAAGTGTGAAA

32/330

**FIGURE 32**

MCSRVP L L L L L L L L L L A L G P G V Q G C P S G C Q C S Q P Q T V F C T A R Q G T T V P R D V P P D T V G L Y V F E N  
G I T M L D A G S F A G L P G L Q L L D L S Q N Q I A S L P S G V F Q P L A N L S N L D L T A N R L H E I T N E T F R G L R  
R L E R L Y L G K N R I R H I Q P G A F D T L D R L L E L K L Q D N E L R A L P P L R L P R L L L L D L S H N S L L A L E P  
G I L D T A N V E A L R L A G L G L Q Q L D E G L F S R L R N L H D L D V S D N Q L E R V P P V I R G L R G L T R L R L A G  
N T R I A Q L R P E D L A G L A A L Q E L D V S N L S L Q A L P G D L S G L F P R L R L L A A A R N P F N C V C P L S W F G  
P W V R E S H V T L A S P E E T R C H F P P K N A G R L L L E L D Y A D F G C P A T T T T A T V P T T R P V V R E P T A L S  
S S L A P T W L S P T A P A T E A P S P P S T A P P T V G P V P Q P Q D C P P S T C L N G G T C H L G T R H H L A C L C P E  
G F T G L Y C E S Q M G Q G T R P S P T P V T P R P P R S L T L G I E P V S P T S L R V G L Q R Y L Q G S S V Q L R S L R L  
T Y R N L S G P D K R L V T L R L P A S L A E Y T V T Q L R P N A T Y S V C V M P L G P G R V P E G E E A C G E A H T P P A  
V H S N H A P V T Q A R E G N L P L L I A P A L A A V L L A A L A A V G A A Y C V R R G R A M A A A A Q D K G Q V G P G A G  
P L E L E G V K V P L E P G P K A T E G G G E A L P S G S E C E V P L M G F P G P G L Q S P L H A K P Y I

33/330

**FIGURE 33**

GAATCATCCACGCACCTGCAGCTCTGCTGAGAGAGTGCAAGCCGTGGGGGTTTTGAGCTCAT  
CTTCATCATTCATATGAGGAAATAAGTGGTAAAATCCTTGGAATACA**ATG**AGACTCATCAG  
AAACATTTACATATTTTGTAGTATTGTTATGACAGCAGAGGGTGATGCTCCAGAGCTGCCAG  
AAGAAAGGGAACCTGATGACCAACTGCTCCAACATGTCTCTAAGAAAGGTTCCCGCAGACTTG  
ACCCAGCCACAACGACACTGGATTTATCCTATAACCTCCTTTTTCAACTCCAGAGTTTCA  
TTTTCATTTCTGTCTCCAAACTGAGAGTTTTGATTCTATGCCATAACAGAATTCAACAGCTGG  
ATCTCAAAACCTTTGAATTCACAAGGAGTTAAGATATTTAGATTTGTCTAATAACAGACTG  
AAGAGTGTAACCTTGGTATTTACTGGCAGGTCTCAGGTATTTAGATCTTTCTTTTAATGACTT  
TGACACCATGCCTATCTGTGAGGAAGCTGGCAACATGTACACCTGGAAATCCTAGGTTTGA  
GTGGGGCAAAAATACAAAATCAGATTTCCAGAAAATTGCTCATCTGCATCTAAATACTGTC  
TTCTTAGGATTCAGAACTCTTCCTCATTATGAAGAAGGTAGCCTGCCCATCTTAAACACAAC  
AAAAGTGCACATTGTTTTACCAATGGACACAAATTTCTGGGTTCTTTTGGGTGATGGAATCA  
AGACTTCAAAAATATTAGAAATGACAAATATAGATGGCAAAAGCCAATTTGTAAGTTATGAA  
ATGCAACGAAATCTTAGTTTGTAGAAAATGCTAAGACATCGGTTCTATTGCTTAATAAAGTTGA  
TTTACTCTGGGACGACCTTTTCTTATCTTACAATTTGTTTGGCATAACATCAGTGGAACT  
TTCAGATCCGAAATGTGACTTTTGGTGGTAAGGCTTATCTTGACCACAATTCATTTGACTAC  
TCAATACTGTAATGAGAAGCTATAAAATTTGGAGCATGTACATTTTCAAGAGTGTTTTACATTCA  
ACAGGATAAAATCTATTTGCTTTTGACCAAAATGGACATAGAAAACCTGACAATATCAAATG  
CACAAATGCCACACATGCTTTTCCCGAATTATCTTACGAAATTTCCAATATTTAAATTTTGGC  
AATAATATCTTAACAGACGAGTTGTTTAAAGAAGCTATCCAAGTGCCTCACTTGAAAAGTCT  
CATTTTGAATGGCAATAAACTGGAGACACTTTCTTTAGTAAGTTGCTTTGCTAACAACACAC  
CCTTGGAACACTTGGATCTGAGTCAAAATCTATTACAACATAAAAATGATGAAAATTTGCTCA  
TGGCCAGAACTGTGGTCAATATGAATCTGTCTACATAAAATTTGCTGATTCTGTCTTCAG  
GTGCTTGCCCAAGTATTCAAATACCTTGACCTAATAATAACCAATTCAAACTGTACCTA  
AAGAGACTATTCATCTGATGGCCTTACGAGAAGCTAAATATTGCATTTAATTTTCTAACTGAT  
CTCCCTGGATGCAGTCATTTCAAGTAGACTTTTCAAGTCTGAACATTGAAATGAAGTTTCAATTCT  
CAGCCCATCTCTGGATTTTGTTCAGAGCTGCCAGGAAGTTAAAGCTCTAAATGCGGGGAAGAA  
ATCCATTCGGGTGTACCTGTGAATTAATAAAATTTTCAATTCAGCTTGAAACATATTCAGAGGTC  
ATGATGGTTGGATGGTCAGATTCACACCTGTGAATACCTTTTAAACCTAAGGGGAAGTAG  
GTTAAAGACGTTTCTCTCCACGAATTATCTTGCAACACAGCTCTGTTGATTGTCAACATTG  
TGGTTATTATGCTAGTTCTGGGGTTGGCTGTGGCCTTCTGCTGTCTCCACTTTGATCTGCCC  
TGGTATCTCAGGATGCTAGGTCAATGCACACAAACATGGCACAGGGTTAGGAAAACAACCCA  
AGAACAACCTCAAGAGAAATGTCCGATTCCACGCAATTTATTTTATACAGTGAACATGATTCTC  
TGTGGGTGAAGAAATGAATTGATCCCCAATCTAGAGAAGGAAGATGGTTCTATCTTGATTGTC  
CTTTATGAAAGCTACTTTGACCCTGGCAAAAGCATTAGTGAAAATATTGTAAGCTTCATTGA  
GAAAAGCTATAAGTCCATCTTTGTTTTGTCTCCCAACTTTGTCCAGAATGAGTGGTGCCATT  
ATGAATTTCTACTTTGCCCACCACAATCTCTTCCATGAAAATTTCTGATCATATAATTTCTTATC  
TTACTGGAACCCATTCCATTCTATTGCATTTCCACCAGGTATCATAAACTGAAAGCTCTCCT  
GGAAAAAAAAGCATACTTGGAATGGCCCAAGGATAGGCGTAAATGTGGGCTTTTCTGGGC  
ACCTTCGAGCTGCTATTAATGTTAATGTATTAGCCACCAGAGAAATGTATGAAGTGCAGACA  
TTCACAGAGTTAAATGAAGAGTCTCGAGGTTCTACAATCTCTCTGATGAGAACAGATTGTCT  
**ATAAAAT**CCCACAGTCCTTGGGAAGTTGGGGACCACATACACTGTTGGGATGTACATTGATA  
CAACCTTTATGATGGCAATTTGACAATATTTATTAATAAAAAATGGTTATTTCCCTTCATA  
TCAGTTTCTAGAAGGATTTCTAAGAATGTATCCTATAGAAACACCTTCACAAGTTTATAAGG  
GCTTATGGAAAAAGGTGTTTCATCCCAGGATTGTTTATAATCATGAAAAATGTGGCCAGGTGC  
AGTGGCTCACTCTTGTAATCCCAGCACTATGGGAGGCCAAGGTGGGTGACCCACGAGGTCAA  
GAGATGGAGACCATCCTGGCCAACATGGTGAAACCTGTCTCTACTAAAAATACAAAAATTA  
GCTGGGCTGATGGTGCACGCCTGTAGTCCCAGCTACTTGGGAGGCTGAGGCAGGAGATCG  
CTTGAACCCGGGAGGTGGCAGTTGCAGTGAGCTGAGATCGAGCCACTGCACTCCAGCCTGGT  
GACAGAGCGAGACTCCATCTCAAAAAAAGAAAAAAGAAAAAATGGAAAAACATCC  
TCATGGCCACAAAATAAGGTCTAATTCAATAAATTATAGTACATTAATGTAATATAATATTA  
CATGCCACTAAAAAGAATAAGGTAGCTGTATATTTCTGGTATGGAAAAACATATTAATAT  
GTTATAACTATTAGGTTGGTGCAAAACTAATTTGTTGGTTTTTGCATTGAAATGGCATTGAA  
ATAAAAGTGTAAGAAATCTATACCAAGTGTAGTAACAGTGGTTTGGGCTGGGAGGTTGGA  
TTACAGGGAGCATTTGATTTCTATGTTGTGTATTTCTATAATGTTTGAATTTGTTTAGAATGA  
ATCTGTATTTCTTTTATAAGTAGAAAAAATAAAGATAGTTTTTACAGCCT

34/330

**FIGURE 34**

MRLIRNIYIFCSIVMTAEGDAPELPEERELMTNCSNMSLRKVPADLTPATTTLDLSYNLLFQ  
LQSSDFHSVSKLRVLILCHNRIQQDLKTFEFNKELRYLDLSNNRLKSVTWYLLAGLRYLDL  
SFNDFDTMPICEEAGNMSHLEILGLSGAKIQKSDFQKIAHLHLNTVFLGFRTLPHYEEGSLP  
ILNTTKLHIVLPMDTNFWVLLRDGIKTSKILEMTNIDGKSQFVSYEMQRNLSLENAKTSVLL  
LNKVDLLWDDLFLILQFVWHTSVEHFQIRNVTFGGKAYLDHNSFDYSNTVMRTIKLEHVHFR  
VFYIQQDKIYLLLTkMDIENLTISNAQMPHMLFPNYPTKFQYLNfANNILTDELfKRTIQLP  
HLKTLILNGNKLETLSLVSCFANNTPLEHLDLsqNLLQHkNDENCsWPETVVNMNLSYNKLS  
DSVFRCLPKSIQILDlnnnQIQTVPKETIHLMAReLNIAfNfLTDLPgCSHFsrLSVLNIE  
MNFILSPSLDFVQSCQEVKTLNAGRNPFRCTCELKNFIQLETYSEVMVGWSDSYTCEYPLN  
LRGTRLKDVHLHELSCNTALLIVTIVVIMLVGLAVAFcCLHFDLPWYLRMLGQCTQTWHRV  
RKTTQEQlKRNVRFHAFISYSEHDSLWVKNELIPNLEKEDGSILICLYESYFDPGKSISENI  
VSFIEKSYKSI FVLSPNFVQNEWCHYEFYFAHhNLFHENSdHIILILLEPIPFYCIPTRYHK  
LKALLEKKAYLEWPKDRRKCGLFWANLRAAINVNVLATREMYELQTFTELNEESRGSTISLM  
RTDCL

35/330

**FIGURE 35**

GGGGGCTTTCTTGGGCTTGGCTGCTTGGAAACACCTGCCTCCAAGGACCGGCCTCGGAGGGGTGCGCGGGAAAGG  
GAGGGAAGAAGGAAGGGCGGGGCGGCCCCCTGCGCCCGCCCGCGCCTCTGCGCGCCCCCTGTCCGCCCCGGC  
CCAGCCCAGCCCAGCCCCGCGGGCCGGTCACACGCGCAGCCGCGCCGCGCCCTCCCGCGCCCAAGCGCGCCGCT  
CTGCTGTGCCCTGCGCCCTTGCCCCGCGCCAGCTTCTGCGCCCGCAGCCCCCGCGCCCGCGTACCCTGA  
CCCTGCCCTGGGCGCGGGGCGGAGCAGGCATGTCCTCCGCGCCGGGACCGCTACCCAGCGCTGGCCCTGGTGCTC  
CTGGCAGTGACCCTGGCCGGGGTCCGAGCCCAGGGCGCAGCCCTCGAGGACCCTGATTATTACGGGCAGGAGAT  
CTGGAGCCGGGAGCCCTACTACGCGCGCCCGGAGCCCGAGCTCGAGACCTTCTCTCCGCGCTGCCTGCGGGGC  
CCGGGGAGGAGTGGGAGCGGCGCCCGCAGGAGCCCAGGCCGCCCAAGAGGGCCACCAAGCCCAAGAAAGCTCCC  
AAGAGGGAGAAGTCCGGCTCCGGAGCCGCTCCACCAGGTAACACAGCAACAAAAAGTTATGAGAACCAAGAG  
CTCTGAGAAGGCTGCCAACGATGATCACAGTGTCCGTGTGGCCCGTGAAGATGTCAGAGAGAGTTGCCACCTC  
TTGGTCTGGAACCTTAAAAATCACAGACTTCCAGCTCCATGCCTCCACGGTGAAGCGCTATGGCCTGGGGCA  
CATCGAGGGAGACTCAACATCCAGGCGGGCATTAAATGAAAATGATTTTTATGACGGAGCGTGGTGCGCGGGAAG  
AAATGACCTCCAGCAGTGGATTGAAGTGGATGCTCGGCGCCTGACCAGATTCACTGGTGTCACTCAAGGGA  
GGAACCTCCCTCTGGCTGAGTGACTGGGTGACATCCTATAAGGTCATGGTGAGCAATGACAGCCACACGTGGGT  
ACTGTTAAGAATGGATCTGGAGACATGATATTTGAGGGAACAGTGAGAAGGAGATCCCTGTTCTCAATGAGCT  
ACCCGTCCCCATGGTGGCCCGCTACATCCGCATAAACCCCTCAGTCTGGTTTGATAATGGGAGCATCTGCATGA  
GAATGGAGATCCTGGGCTGCCACTGCCAGATCCTAATAATTATTATCACCGCCGGAACGAGATGACCACCT  
GATGACCTGGATTTTAAGCACCACAATTATAAGGAAATGCGCCAGTTGATGAAAGTTGTGAATGAAATGTGTCC  
CAATATCACCAAGATTTACAACATTGGAAAAAGCCACCAGGGCCTGAAGCTGTATGCTGTGGAGATCTCAGATC  
ACCTGGGGAGCATGAAGTCGGTGAGCCCCGAGTTCCTACTACATCGCGGGGGGCCACGGCAATGAGGTGCTGGGC  
CGGGAGCTGCTGCTGCTGCTGGTGACGTTCTGTGTGTCAGGAGTACTTGGCCCGGAATGCGCGCATCTGCACCT  
GGTGGAGGAGACGCGGATTACGTCCTCCCTCCCTCAACCCCGATGGCTACGAGAAGGCCTACGAAGGGGGCT  
CGGAGCTGGGAGGCTGGTCCCTGGGACGCTGGACCCACGATGGAATTGACATCAACAACAACCTTTCCTGATTTA  
AACACGCTGCTCTGGGAGGCAGAGGATCGACAGAATGTCCCAGGAAAGTTCCCAATCACTATATTGCAATCCC  
TGAGTGGTTTTCTGTGCGGAAATGCCACGGTGGCTGCCGAGACCAGAGCAGTCATAGCCTGGATGGAAAAATCC  
CTTTGTGCTGGGCGGCAACCTGCAGGGCGGCGAGCTGGTGGTGGCGTATCCCTACGACCTGGTGCGGTCCCC  
TGGAAGACGCAGGAACACACCCCCACCCCGATGACCACGTGTTCCGCTGGCTGGCTACTCCTATGCCTCCAC  
ACACCGCCTCATGACAGACGCCCCGAGGAGGGTGTGCCACACGGAGGACTTCCAGAAGGAGGAGGGCACTGTCA  
ATGGGGCCTCCTGGCACACCGTCGCTGGAAGTCTGAACGATTTAGCTACCTTCATACAACTGCTTCGAACTG  
TCCATCTACGTGGGCTGTGATAAATACCCACATGAGAGCCAGCTGCCCGAGGAGTGGGAGAATAACCGGGAATC  
TCTGATCGTGTTCATGGAGCAGGTTTCATCGTGGCATTAAAGGCTTGGTGAGAGATTACATGGAAAAGGAATCC  
CAAACGCCATTATCTCCGTAGAAGGCATTAACCATGACATCCGAACAGCCAACGATGGGGATTACTGGCGCCTC  
CTGAACCTGGAGAGTATGTGGTCACAGCAAAGGCGAAGTTTCACTGCATCCACCAAGAACTGTATGGTTGG  
CTATGACATGGGGGCCACAAGGTGTGACTTCACACTTAGCAAAACCAACATGGCCAGGATCCGAGAGATCATGG  
AGAAGTTTGGGAAGCAGCCCGTCAGCCTGCCAGCCAGGCGGCTGAAGCTGCGGGGGCGGAAGAGACGACAGCGT  
GGGTGACCCCTCCTGGGCCCTTGAGACTCGTCTGGGACCCATGCAATTAAACCAACCTGGTAGTAGCTCCATAG  
TGGACTCACTCACTGTTGTTTCTCTGTAATTCAGAAGTGCCTGGAAGAGAGGGTGCATTGTGAGGCAGGTCC  
CAAAGGGAAGGCTGGAGGCTGAGGCTGTTTTCTTTCTTTGTTCCCATTTATCCAAATAACTTGGACAGAGCA  
GCAGAGAAAAGCTGATGGGAGTGAGAGAACTCAGCAAGCCAACCTGGGAATCAGAGAGAGAAGGAGAAGGAGGG  
GAGCCTGTCCGTTCAAGACCTCTGGCTGCATAGAAAAGGATTCTGGTGCTTCCCTGTTGCGTGGCAGCAAGG  
GTTCCACGTGCATTTGCAATTTGCACAGCTAAAATTGCAGCATTTCCCGAGCTGGGCTGTCCCAATGTTACCA  
TTTGAGATGCTCCAGGCGTCCTAAGAGAATCCACCCTCTCTGGCCCTGGGACATTGCAAGCTGCTACAAATAA  
ATTCTGTGTTCTTTTGACAATAGCGTCATTGCCAAGTGACATCAGTGAGCCTCTTGAATCTGTTTAGTCTCCT  
TTTTCAACAAAGGAGTGTGTTTCAAGAAAAGGAGAGAGAGGCTGAGATCATTAGGAGTTGTTGGGCAGCAAGCA  
TGGAGCTTCTTGACAAATTCTGGGTCCATAAACAACCCCAAGTCCCTGCTGATCCAGTAGCCCTGGAGGTT  
CCCCAGGTAGGGAGAGCCAGAGGTGCCAGCCTTCTGAAGGGCCAGAAAATTTAGCCTGGATCTCCTCTTTTAC  
CTGCTAGGACTGGAAGAGCCAGAAGTGGGGTGGCCTGAAGCCCTCTCTGCTTGGGTATTGCCCTGTGTG  
GAATTGAGTGCTCATGGGTTGGCCTCATATCAGCCTGGGAGTTATTTTTGATATGTAGAATGCCAGATCTTCCA  
GATTAGGCTAAATGTAATGAAAACCTCTTAGGATTATCTGTGGAGCATCAGTTTGGGAAGAATTATTGAATTAT  
CTTGCAAGAAAAAGTATGTCTCACTTTTTGTTAATGTTGCTGCCTCATTGACCTGGGAAAAATGAAAAAAA  
AATAAAGCAAATGGTAAGACCCTTAAAAAAA



36/330

**FIGURE 36**

MSRPGTATPALALVLLAVTLAGVGAQGALEDPDYYGQEIWSREPYARPEPELETFSPPLP  
AGPGEEWERRPQEP RPPK R A T K P K K A P K R E K S A P E P P P P G K H S N K K V M R T K S S E K A A N D D H S  
VRVAREDVRESC P P L G L E T L K I T D F Q L H A S T V K R Y G L G A H R G R L N I Q A G I N E N D F Y D G A W C A  
GRNDLQQWIEVDARRLTRFTGVITQGRNSLWLSDWVTSYKVMVSNDSHTWVTVKNGSGDMIF  
EGNSEKEIPVLNELPVPMPVARYIRINPQSWFDNGSICMRMEILGCPLPDPNNYYHRRNEMTT  
TDDLDFKHHNYKEMRQLMKVVNEMCPNITRIYNIGKSHQGLKLYAVEISDHPGEHEVGEPEF  
HYIAGAHGNEVLGRELLLLLVQFVCQEYLARNARIVHLVEETRIHVLPSLNP DGYEKAYEGG  
SELGGWSLGRWTHDGIDINNNFPDLNTLLWEAEDRQNVPRKVPNHYIAIPEWFLSENATVAA  
ETRAVIAWMEKIPFVLGGNLQGGELVVAYPYDLVRSPWKTQEHTPTPDDHVFRWLAYS YAST  
HRLMTDARRRVCHTEDFQKEEGTVNGASWHTVAGSLNDFS YLHTNCFELSIYVGCDKYPHES  
QLPEEWENNRESLIVFMEQVHRGIKGLVRDSHGKGIPNAIISVEGINHDIRTANDGDYWRL  
NPGEYVVTAKAEGFTASTKNCMVGYDMGATRCDFTL SKTNMARI REIMEKFGKQPVSLPARR  
LKLGRGRRRQRG

37/330

**FIGURE 37**

CTAAGAGGACAAG**ATG**AGGCCCGGCCTCTCATTCTCCTAGCCCTTCTGTTCTTCCTTGGCCAAGCTGCAGGGG  
ATTTGGGGGATGTGGGACCTCCAATTCCCAGCCCCGGCTTCAGCTCTTTCCCAGGTGTTGACTCCAGCTCCAGC  
TTCAGCTCCAGCTCCAGGTCCGGGCTCCAGCTCCAGCCGAGCTTAGGCAGCGGAGGTTCTGTGTCCAGTTGTT  
TTCCAATTTACCCGGCTCCGTGGATGACCGTGGGACCTGCCAGTGCTCTGTTTCCCTGCCAGACACCACCTTTC  
CCGTGGACAGAGTGGAACGCTTGAATTCACAGCTCATGTTCTTTCTCAGAAGTTTGAGAAAGAACTTTCTAAA  
GTGAGGGAATATGTCCAATTAATTAGTGTGTATGAAAAGAACTGTTAAACCTAACTGTCCGAATTGACATCAT  
GGAGAAGGATACCATTTCTTACACTGAACTGGACTTCGAGCTGATCAAGGTAGAAGTGAAGGAGATGGAAAAAC  
TGGTCATACAGCTGAAGGAGAGTTTTGGTGGAAAGCTCAGAAATTGTTGACCAGCTGGAGGTGGAGATAAGAAAT  
ATGACTCTCTTGGTAGAGAAGCTTGAGACACTAGACAAAAACAATGTCTTGCCATTCGCCGAGAAATCGTGGC  
TCTGAAGACCAAGCTGAAAGAGTGTGAGGCCTCTAAAGATCAAAACACCCCTGTCGTCCACCCTCCTCCCACTC  
CAGGGAGCTGTGGTCATGGTGGTGTGGTGAACATCAGCAAACCGTCTGTGGTTCAGCTCAACTGGAGAGGGTTT  
TCTTATCTATATGGTGCTTGGGGTAGGGATTACTCTCCCCAGCATCCAAACAAAGGACTGTATTGGGTGGCGCC  
ATTGAATACAGATGGGAGACTGTTGGAGTATTATAGACTGTACAACACACTGGATGATTTGCTATTGTATATAA  
ATGCTCGAGAGTTGCGGATCACCTATGGCCAAGGTAGTGGTACAGCAGTTTACAACAACAACATGTACGTCAAC  
ATGTACAACACCGGAATATTGCCAGAGTTAACCTGACCACCAACACGATTGCTGTGACTCAAACCTCTCCCTAA  
TGCTGCCTATAATAACCGCTTTTTCATATGCTAATGTTGCTTGGCAAGATATTGACTTTGCTGTGGATGAGAATG  
GATTGTGGGTTATTTATTCAACTGAAGCCAGCACTGGTAACATGGTGATTAGTAAACTCAATGACACCACACTT  
CAGGTGCTAAACACTTGGTATACCAAGCAGTATAAACCATCTGCTTCTAACGCCTTCATGGTATGTGGGGTTCT  
GTATGCCACCCGTACTATGAACACCAGAACAGAAGAGATTTTTTACTATTATGACACAAACACAGGGAAAGAGG  
GCAAACTAGACATTGTAATGCATAAGATGCAGGAAAAAGTGCAGAGCATTAACATAACCCTTTTGACCAGAAA  
CTTTATGTCTATAACGATGGTTACCTTCTGAATTATGATCTTTCTGTCTTGCAAGAGCCCG**TAAG**CTGTTTA  
GGAGTTAGGGTGAAAGAGAAAAATGTTTGTGAAAAAATAGTCTTCTCCACTTACTTAGATATCTGCAGGGGTGT  
CTAAAAGTGTGTTCAATTTTGCAGCAATGTTTAGGTGCATAGTTCTACCACACTAGAGATCTAGGACATTTGTCT  
TGATTTGGTGAGTTCTCTTGGGAATCATCTGCCTCTTCAGGCGCATTTTGCAATAAAGTCTGTCTAGGGTGGGA  
TTGTCAGAGGTCTAGGGGCACTGTGGGCCTAGTGAAGCCTACTGTGAGGAGGCTTCACTAGAAGCCTTAAATTA  
GGAATTAAGGAACCTTAAACTCAGTATGGCGTCTAGGGATTCTTTGTACAGGAAATATTGCCCAATGACTAGTC  
CTCATCCATGTAGCACCCTAATTCTTCCATGCCTGGAAGAAACCTGGGGACTTAGTTAGGTAGATTAATATCT  
GGAGCTCCTCGAGGGACCAAATCTCCAACCTTTTTTTTCCCCTCACTAGCACCTGGAATGATGCTTTGTATGTGG  
CAGATAAGTAAATTTGGCATGCTTATATATTCTACATCTGTAAAGTGCTGAGTTTTATGGAGAGAGGCCTTTTT  
ATGCATTAAATTGTACATGGCAAATAAATCCAGAAGGATCTGTAGATGAGGCACCTGCTTTTTCTTTCTCTC  
ATTGTCCACCTTACTAAAAGTCAGTAGAATCTTCTACCTCATAACTTCCTTCCAAAGGCAGCTCAGAAGATTAG  
AACCAGACTTACTAACCAATTCCACCCCCCAACCCCTTCTACTGCCTACTTTAAAAAATTAATAGTTTT  
CTATGGAAGTATCTAAGATTAGAAAAATTAATTTCTTTAATTTTATTATGGACTTTTATTTACATGACTCTA  
AGACTATAAGAAAAATCTGATGGCAGTGACAAAGTGCTAGCATTTATTGTTATCTAATAAAGACCTTGGAGCATA  
TGTGCAACTTATGAGTGTATCAGTTGTTGCATGTAATTTTTGCTTTGTTTAAGCCTGGAACCTGTAAGAAAT  
GAAAATTTAATTTTTTTTTCTAGGACGAGCTATAGAAAAGCTATTGAGAGTATCTAGTTAATCAGTGCAGTAGT  
TGGAAACCTTGCTGGTGTATGTGATGTGCTTCTGTGCTTTTGAATGACTTTATCATCTAGTCTTTGTCTATTTT  
TCCTTTGATGTTCAAGTCCTAGTCTATAGGATTGGCAGTTTAAATGCTTTACTCCCCCTTTTAAATAAATGAT  
TAAAATGTGCTTTGAAAAAATAAAAAAAAAAAAAAAAAAAAAA

38/330

**FIGURE 38**

MRPGLSFLLALLFFLGQAAGDLGDVGPPPIPSPGFSSFPGVDSFFFSSSSSRGSSSSSRSLGS  
GGSVSQLFSNFTGSVDDRGTCQCSVSLPDTTFPVDRVERLEFTAHVLSQKFEKELSKVREYV  
QLISVYEKKLLNLTVRIDIMEKDTISYTELDFELIKVEVKEMEKLVIQLKESFGGSSEIVDQ  
LEVEIRNMTLLVEKLETLDKNNVLAIRREIVALKTKLKECEASKDQNTPVVHPPPTPGSCGH  
GGVVNISKPSVVQLNWRGFSYLYGAWGRDYSPQHHPNKGLYWVAPLNTDGRLLLEYRLYNTLD  
DLLLYINARELRITYGQGSGTAVYNNNMYVNMVNTGNIARVNLTNTIAVTQTLPNAAYNNR  
FSYANVAWQDIDFAVDENGLWVIYSTEASTGNMVISKLNDDTLQVLNTWYTKQYKPSASNAF  
MVCGLVLYATRTMNTRTEEIFYYYDTNTGKEGKLDIVMHKMQEKVQSINYNPFDQKLYVYNDG  
YLLNYDLSVLQKPQ

39/330

**FIGURE 39**

GCTCTGAAGACCAAGCTGAAAGAGTGTGAGGCCTCTAAAGATCAAACACCCCTGTCGTCCAC  
CCTCCTCCCCTCCAGGGAGCTGTGGTCATGGTGGTGTGGTGAACATCAGCAAACCGTCTGT  
GGTTCAGCTCAACTGGAGAGGGTTTTCTTATCTATATGGTGCTTGGGGTAGGGATTACTCTC  
CCCAGCATCCAAACAAAGGNATGTATTGGGNGGCGCCATTGAATACAGATGGGAGACTGTTG  
GAGTATTATAGACTGTACAACCCACTGGATGATTTGCTATTGTATATAAATGCTCGAGAGTT  
GCGGATCACCTATGGCCAAGGTAGTGGTACAGCAGTTTACAACAACAACATGTACGTCAACA  
TGTACAACACCGGNATATTGCCAGAGTTAACCTGACC

40/330

**FIGURE 40**

TCTCGCAGATAGTAAATAATCTCGGAAAGGCGAGAAAGAAGCTGTCTCCATCTTGTCTGTAT  
CCGCTGCTCTTGTGACGTTGTGGAG**ATG**GGGGAGCGTCCTGGGGCTGTGCTCCATGGCGAGCT  
GGATACCATGTTTGTGTGGAAGTGCCCCGTGTTTGCTATGCCGATGCTGTCTAGTGGAAC  
AACTCCACTGTAAC TAGATTGATCTATGCACTTTTCTTGCTTGTTGGAGTATGTGTAGCTTG  
TGTAATGTTGATACCAGGAATGGAAGAACAACCTGAATAAGATTCCTGGATTTTGTGAGAATG  
AGAAAGGTGTTGTCCCTTGTAACATTTTGGTTGGCTATAAAGCTGTATATCGTTTGTGCTTT  
GGTTTGGCTATGTTCTATCTTCTTCTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGA  
TCCTAGAGCTGCAGTGCACAATGGATTTTGGTTCTTTAAATTTGCTGCAGCAATTGCAATTA  
TTATTGGGGCATTCTTCATTCCAGAAGGAACCTTTTACAACCTGTGTGGTTTTATGTAGGCATG  
GCAGGTGCCTTTTGTTCATCCTCATAACAACCTAGTCTTACTTATTGATTTTGCACATTCATG  
GAATGAATCGTGGGTGAAAAAATGGAAGAAGGGAACCTCGAGATGTTGGTATGCAGCCTTGT  
TATCAGCTACAGCTCTGAATTATCTGCTGTCTTTAGTTGCTATCGTCCTGTTCTTTGTCTAC  
TACACTCATCCAGCCAGTTGTTTCAAGAAAACAGGCGTTTATCAGTGTCAACATGCTCCTCTG  
CGTTGGTGCTTCTGTAATGTCTATACTGCCAAAAATCCAAGAATCACAACCAAGATCTGGTT  
TGTTACAGTCTTCAGTAATTACAGTCTACACAATGTATTTGACATGGTCAGCTATGACCAAT  
GAACCAGAAACAAATTGCAACCCAAGTCTACTAAGCATAATTGGCTACAATACAACAAGCAC  
TGTCCTCAAAGGAAGGGCAGTCAGTCCAGTGGTGGCATGCTCAAGGAATTATAGGACTAATTC  
TCTTTTGTGTGTGTATTTTATTCCAGCATCCGTAACCTCAAACAATAGTCAGGTTAATAAA  
CTGACTCTAACAAAGTGATGAATCTACATTAATAGAAGATGGTGGAGCTAGAAGTGATGGATC  
ACTGGAGGATGGGGACGATGTTTCAACGAGCTGTAGATAATGAAAGGGATGGTGTCACTTACA  
GTTATTCCTTCTTTCACCTTCATGCTTTTCTGGCTTCACTTTATATCATGATGACCCTTACC  
AACTGGTCCAGGTATGAACCTCTCGTGAGATGAAAAGTCAGTGGACAGCTGTCTGGGTGAA  
AATCTCTTCCAGTTGGATTGGCATCGTGCTGTATGTTTGGACACTCGTGGCACCCTTGTTC  
TTACAAATCGTGATTTT**GACTGAGT**GAGACTTCTAGCATGAAAGTCCCCTTTGATTATTGC  
TTATTTGAAAACAGTATTCCCAACTTTTGTAAAGTTGTGTATGTTTTTGTCTCCCATGTAAAC  
TTCTCCAGTGTTCTGGCATGAATTAGATTTTACTGCTTGTCAATTTTGTATTTTCTTACCAA  
GTGCATTGATATGTGAAGTAGAATGAATTGCAGAGGAAAGTTTTATGAATATGGTGATGAGT  
TAGTAAAAGTGGCCATTATTGGGCTTATTCTCTGCTCTATAGTTGTGAAATGAAGAGTAAAA  
ACAAATTTGTTTGACTATTTTAAAATTATATTAGACCTTAAGCTGTTTTAGCAAGCATTAAA  
GCAAATGTATGGCTGCCTTTTGAATATTTGATGTGTTGCCTGGCAGGATACTGCAAAGAAC  
ATGGTTTTATTTTAAAATTTATAACAAGTCACTTAAATGCCAGTTGTCTGAAAAATCTTATA  
AGGTTTTACCCTTGATACGGAATTTACACAGGTAGGGAGTGTTTAGTGGACAATAGTGTAGG  
TTATGGATGGAGGTGTCCGTACTAAATTGAATAACGAGTAAATAATCTTACTTGGGTAGAGA  
TGGCCTTTGCCAACAAAGTGAACCTGTTTTGGTTGTTTTAAACTCATGAAGTATGGGTTTCACT  
GGAAATGTTTGAACCTCTGAAGGATTTAGACAAGGTTTTGAAAAGGATAATCATGGGTTAGA  
AGGAAGTGTTTTGAAAGTCACTTTGAAAGTTAGTTTTGGGCCAGCACGGTAGCTCACCCTT  
GGTAATCCCAGCACTTTGGGAGCTTAAGTGGGTAGATTACTTGAGCCCAGGAATTCAGACCA  
GCTTGGCACATGGTGAACCTGTTCTATAAAAAATAATCTGGCTTTGAGCATATGCCTGTGGTC  
CAGCACTGAGAGGCTAGTGAAGATTGCTGAGCCCAGAGCCAAAGGTTGCAGTGAGCAAGTCA  
CGTCACTGCACTCTAGCTGGCACAGAGTAAGCCAAAAAATATATATATATTGAAATCAAGG  
AGGCAAAATTTTACAGGGAAGGAAGTAACCTGCAAAACCACTAGGCTTTAGTAGGTACTTAT  
ATAAAATCTAGTCCAGTTCTCTCATTTAAAAAATGAAGACACTGAAATACAGACTTAAATA  
GCTCAGATAGCTAATTAGGAAATTTCAAGTTGGCCAATAATAGCATTCTCTCTGACATTTAA  
AAATAATTTCTATTCAAAATACATGCATATTGATTTACACCTCATACTGTGATAATTAATGT  
GATGTGGATTGCTGGTGTCCAGCATGACCCATAAACAGGTCAGAAGAATGATGGAATGTTTT  
AGAATAAACTCCTGCTTATAGTATACTACACAGTTCAAAGATGTTTAAATGCTTTTGTAT  
TTACTGCCATGTAATTGAAATATATAGATTATTGTAACCTTTCAACCTGAAAATCAAGCAGT  
ATGAGAGTTTATTTATTTGTATGTCTACTAGTGTCTAATGAAGCTTTTAAATCTACAATT  
TCTTCTTTAAAAATTTTATTAATGTGAATGGAATATAACAATTCAGCTTAAATCCCCAACCC  
TTATTCTGTGTGTAGACATTGTATTCCACAATTTTGAATGGCTGTGTTTTACCTCTAAATAA  
ATGAATTCAGAGAAAAA

41/330

**FIGURE 41**

MGSVLGLCSMASWIPCLCGSAPCLLCRCCPSGNNSTVTRLIYALFLLVGVCVACVMLIPGME  
EQLNKIPGFCENEKGVVPCNILVGKAVYRLCFGLAMFYLLLSLLMIKVKSSSDPRAAVHNG  
FWFFKFAAAIAIIIGAFFIPEGTFTTVWFYVGMAGAFCFILIQVLVLLIDFAHSWNESWVEKM  
EEGNSRCWYAALLSATALNYLLSLVAIVLFFVYYTHPASCSSENKAFISVNMLLCVGASVMSI  
LPKIQESQPRSGLLQSSVITVYTMYLTSAMTNEPETNCNPSLLSIIGYNTTSTVPKEGQSV  
QWWHAQGIIGLILFLLCVFYSSIRTSNNSQVNKLTLTSDESTLIEDGGARSDGSLEDGDDVH  
RAVDNERDGVITYSYFFHFMLFLASLYIMMTLTNWSRYEPSREMKSQWTAVWVKISSWIGI  
VLYVWTLVAPLVLTNRDFD

42/330

**FIGURE 42**

GCGAGAAAGAAGCTGTCTCCATCTTGTCTGTATCCCGCTGCTTCTTGNGACGTTGTGGAGAT  
GGGGAGCGTCCCTGGGGCTGTGCTCCATGGCGAGCTGGATACCATGTTTGTGTGGAAGTGCC  
CCGTGTTTGCTATGCCGATGCTGTCCTAGTGGAAACAANTCCACTGTAAC TAGATTGATCTA  
TGCACTTTTCTTGCTTGTTGGAGTATGTGTAGCTTGTGTAATGTTGATACCAGGAATGGAAG  
AACAACTGAATAAGATTCCTGGATTTTGTGAGAATGAGAAAGGTGTTGTCCCTTGTAACATT  
TTGGTTGGCTATAAAGCTGTATATCGTTTGTGCTTTGGTTTGGCTATGTTCTATCTTCTTCT  
CTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCAGTGCACAATGGAT  
TTTGGTTCTTTAAATTTGCTGCAGCAATTGCAATTATTATTGGGGC

43/330

**FIGURE 43**

GTTATTGTGAACTTTGTGGAGATGGGAGGTCNTGGGGCTGTGTTCCATGGCGAGCTGGATAC  
CANGTTTGTGTGGAAGTGCCCCGTGTTTGNTATGCCGATGCTGTCCTAGTGGAACAANTCC  
ACTGTAATTAGATTGATNTATGCACTTTTNTTGCTTGTTGGAGTANGTGTAGCTTGTGTAAT  
GTTGATACCAGGAATGGAAGAACAACCTGAATAAGATTCCTGGATTTTGTGAGAATGAGAAAG  
GTGTTGTCCCTTGTAACATTTTGGTTGGCTATAAAGCTGTATATNGTTTGTGCTTTGGTTTG  
GCTANGTTCTATNTTCTTCTCTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAG  
AGCTGCAGTGCACAATGGATTTTGGTTTTTTAAATTTGCTGCAGCAATTGCAATTATTATTG  
GGGC



44/330

**FIGURE 44**

AAGAAGCTGTCTCCATCTTGTCTGTATCCGCTGCTCTTGTGAACGTTNTGGAGATGGGGAGC  
GTCCTTGGGGTTGTGCTCCATGGCGAGCTGGATAACCATGTTTGTGTGGAAGTGCCCCGTGTT  
TGCTATGCCGATGCTGTCCTAGTGGAAACAACCTCCACTGTAACTAGATTGATCTATGCACTT  
TTCTTGCTTGTTGGAGTATGTGTAGCTTGTGTAATGTTGATACCAGGAATGGAAGAACAACCT  
GAATAAGATTCCTGGATTTTGTGAGAATGAGAAAGGTGTTGTCCCTTGTAACATTTTGGTTG  
GCTATAAAGCTGTATATCGTTTGTGCTTTGGTTTGGCTATGTTCTATCTTCTTCTCTCTTTA  
CTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCAGTGCACAATGGATTTTGGTT  
CTTTAAATTTGCTGCAGCAATTGCAATTATTATTGGGGC

45/330

**FIGURE 45**

GCTGTCCTTAGTGGAACAANTCCAACCTTGTAACCTGGATTGATCTATGCACTTTTTTCCTTG  
CTTGTTGGAGTATGTGTAGCTTTGTGTAATGTTGTTCCCAGGATTGGANGAACAACTGAATA  
AGATTCCTGGATTTTTGTGAGAATGAGAAAGGTGTTGTCCCCTTGTAACATTTTTGGTTGGC  
TATAAAGCTGTATATCGTTTGTGCTTTGGTTTGGCTATGTTCTATCTTCTTCTCTTTACT  
AATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCAGTGCACAATGGATTTTGGTTCT  
TTAAATTTGCTGCAGCAATTGCAATTATTATTGGGGCATTCTTCATTCCAGAAGGAACCTTT  
ACAACTGTGTGGTTTTATGTAGGCATGGCAGGTGCCTTTTGTTCATCCTCATACAACTAGT  
CTTACTTATTGATTTTGCACATTCATGGAATGAATCGTGGGTGAAAAAATGGAAGAAGGGA  
ACTCGAGATGTTGGTATGCAGCCTTGTTATCAGCTACAGCTCTGAATTATCTGCTGTCTTTA  
GTTGCTATCGTCCTGTTCTTTGTCTACTACACTCATCCAGCCAGTTGTTTCAGAAAACAAGGC  
GTTTCATCAGTGTCAACATGCTCCTCTGCGTTGGTGCTTCTGTAATG

46/330

**FIGURE 46**

CTCGGGCGCGCACAGGCAGCTCGGTTTGCCTGCGATTGAGCTGCGGGTCGCGGCCGGCGCCGGCCTCTCCAAT  
GGCAATGTGTGTGGCTGGAGGCGAGCGCGAGGCTTTTCGGCAAAGGCAGTCGAGTGTTCGAGACCGGGGCGAG  
TCCTGTGAAAGCAGATAAAAGAAAACATTTATTAACGTGTATTACGAGGGGAGCGCCCGGGGCTGTGCG  
ACTCCCCGCGGAACATTTGGCTCCCTCCAGCTCCGAGAGAGGAGAAGAAGAAAGCGGAAAAAGGCAGATTAC  
GTCGTTTCCAGCCAAGTGGACCTGATCGATGGCCCTCTGAATTTATCACGATATTTGATTTATTAGCGATGCC  
CCCTGGTTTGTGTGTTACGCACACACACGTGCACACAAGGCTCTGGCTCGCTTCCCTCCCTCGTTTCCAGCTCC  
TGGGCGAATCCACATCTGTTTCAACTCTCCGCCGAGGGCGAGCAGGAGCGAGAGTGTGTCGAATCTGCGAGTG  
AAGAGGGACGAGGGAAAAGAAACAAAGCCACAGACGCAACTTGAGACTCCCGCATCCCAAAAGAAGCACCAGAT  
CAGCAAAAAAAGAAGATGGGGCCCCCGAGCCTCGTGCTGTGCTTGTGCTGCCGCAACTGTGTTCTCCCTGCTGGG  
TGGAAGCTCGGCCTTCTGTGTCGCACCAACCGCTGAAAGGCAGGTTTCAGAGGGACCGCAGGAACATCCGCCCA  
ACATCATCTTGGTGTGACGGACGACCAGGATGTGGAGCTGGGTTCCATGCAGGTGATGAACAAGACCCGGCGC  
ATCATGGAGCAGGGCGGGGCGCACTTCATCAACGCCTTCGTGACCACACCCATGTGCTGCCCTCAGCTCCTC  
CATCTCACTGGCAAGTACGTCCACAACCACAACACCTACACCAACAATGAGAACTGCTCCTCGCCCTCCTGGC  
AGGCACAGCAGAGAGCCGCACCTTTGCCGTGTACCTCAATAGCACTGGCTACCGGACAGCTTTCTTCGGGAAG  
TATCTTAATGAATACAACGGCTCCTACGTGCCACCCGGCTGGAAGGAGTGGGTGCGACTCCTTAAAACTCCCG  
CTTTTATAACTACACGCTGTGTGCGAACGGGGTGAAAGAGAAGCACGGCTCCGACTACTCCAAGGATTACCTCA  
CAGACCTCATACCAATGACAGCGTGAGCTTCTTCGCGACGTCCAAGAAGATGTACCCGCACAGGCCAGTCTCTC  
ATGGTCATCAGCCATGCAGCCCCCACGGCCCTGAGGATTCAGCCCCACAATATTCACGCCTCTTCCCAAACGC  
ATCTCAGCACATCAGCCGAGCTACAACCTACGCGCCCAACCCGGACAAACACTGGATCATGCGCTACACGGGGC  
CCATGAAGCCCATCCACATGGAATTCACCAACATGCTCCAGCGGAAGCGCTTGCAGACCCCTCATGTGGTGGAC  
GACTCCATGGAGACGATTTACAACATGCTGGTTGAGACGGCGAGCTGGACAACACGTACATCGTATACACCGC  
CGACCACGGTTACCACATCGGCCAGTTTGGCCTGGTGAAAGGGAATCCATGCCATATGAGTTTGACATCAGGG  
TCCCGTTCTACGTGAGGGGCCCCAACGTGGAAGCCGGCTGTCTGAATCCCCACATCGTCTCAACATTGACCTG  
GCCCCACCATCCTGGACATTGCAGGCCTGGACATACCTGCGGATATGGACGGGAAATCCATCCTCAAGCTGCT  
GGACACGGAGCGGGCGGTGAATCGGTTTCACTTGAAAAAGAAGATGAGGGTCTGGCGGGACTCCTTCTTGGTGG  
AGAGAGGCAAGCTGCTACACAAGAGAGACAATGACAAGGTGGACGCCAGGAGGAGAACTTTCTGCCCAAGTAC  
CAGCGTGTGAAGGACCTGTGTACGCGTGTGAGTACCAGACGGCGTGTGAGCAGCTGGGACAGAAGTGGCAGTG  
TGTGGAGGACGCGACGGGGAAGCTGAAGCTGAGTGAAGGTCGAAGGGCCCCATGCGGCTGGGCGGCAGCAGAGCCC  
TCTCCAACCTCGTGCCCAAGTACTACGGGCAGGGCAGCGAGGCCTGCACCTGTGACAGCGGGGACTACAAGCTC  
AGCCTGGCCGACGCCGGAACCTCTTCAAGAAGAAGTACAAGGCCAGCTATGTCCGCAGTCGCTCCATCCG  
CTCAGTGGCCATCGAGGTGGACGGCAGGGTGTACCACGTAGGCCTGGGTGATGCCGCCAGCCCCGAAACCTCA  
CCAAGCGGCACTGGCCAGGGGCCCCCTGAGGACCAAGATGACAAGGATGGTGGGACTTCAGTGGCACTGGAGGC  
CTTCCCGACTACTCAGCCGCCAACCCCAATTAAGTGACACATCGGTGCTACATCCTAGAGAACGACACAGTCCA  
GTGTGACCTGGACCTGTACAAGTCCCTGCAGGCCTGGAAGACCACAAGCTGCACATCGACCACGAGATTGAAA  
CCCTGCAGAACAAAATTAAGAACCTGAGGGAAAGTCCGAGGTACCTGAAGAAAAAGCGGCCAGAAGAATGTGAC  
TGTCACAAAATCAGCTACCACACCCAGCACAAAGGCCGCTCAAGCACAGAGGCTCCAGTCTGCATCCTTTTCAG  
GAAGGGCTGCAAGAGAAGGACAAGGTGTGGCTGTGCGGGAGCAGAAGCGCAAGAAGAAACTCCGCAAGCTGC  
TCAAGCGCCTGCAGAACACGACACGTGCAGCATGCCAGGCCTCACGTGCTTCACCCACGACAACCAGCACTGG  
CAGACGGCGCCTTTCTGGACACTGGGGCCTTCTAAGTGTGCTGCACCGCCCAACAATAACACGTACTGGTGCAT  
GAGGACCATCAATGAGACTACAATTTCTCTGTGAATTTGCAACTGGCTTCTAGAGTACTTTGATCTCA  
ACACAGACCCCTACCAGCTGATGAATGCAGTGAACACACTGGACAGGGATGTCTCAACCAGCTACACGTACAG  
CTCATGGAGCTGAGGAGCTGCAAGGGTTACAAGCAGTGTAAACCCCGGACTCGAAACATGGACCTGGATGGAGG  
AAGCTATGAGCAATACAGGCAGTTTCAGCGTCGAAAGTGGCCAGAAATGAAGAGACCTTCTTCCAAATCACTGG  
GACAACTGTGGGAAGGCTGGGAAGGTTAAGAAACAACAGAGGTGGACCTCCAAAAACATAGAGGCATCACCTGA  
CTGCACAGGCAATGAAAAACCATGTGGGTGATTTCCAGCAGACCTGTGCTATTGGCCAGGAGGCCTGAGAAAGC  
AAGCAGCACTCTCAGTCAACATGACAGATTCTGGAGGATAACCAGCAGGAGCAGAGATAAAGTTCAGGAAGTCC  
ATTTTTGCCCCGTGCTTTTGGATTATACCTCACCAGCTGCACAAAATGCATTTTTTCGTATCAAAAAGTC  
ACCACTAACCTCCCCAGAAGCTCACAAAGGAAAACGGAGAGAGCGAGCGAGAGAGATTTCTTGGAATTTTC  
TCCCAAGGGCGAAAGTCATTGGAATTTTTAAATCATAGGGGAAAAGCAGTCCTGTTCTAAATCCTCTTATTCTT  
TTGGTTTGTACAAAGAAGGAATAAGAAGCAGGACAGAGGCAACGTGGAGAGGCTGAAAACAGTGCAGAGACG  
TTTGACAATGAGTCAGTAGCACAAAAGAGATGACATTTACCTAGCACTATAAACCTGGTTGCCTCTGAAGAAA  
CTGCCTTCAATTGTATATGTGACTATTTACATGTAATCAACATGGGAACCTTTTAGGGGAACCTAATAAGAAAT  
CCCAATTTTCAGGAGTGGTGGTGTCAATAAACGCTCTGTGGCCAGTGTAAAGAAAAA

47/330

**FIGURE 47**

MGPPSLVLCLLSATVFSLLGGSSAFLSHHRLKGRFQRRNIRPNIIILVLTDDQDVELGSMQ  
VMNKTRRIMEQGGAHFINAFVTTMCCPSRSSILTGKYVHNHNTYTNNECSPSWQAQHE  
RTFAVYLNSTGYRTAFFGKYLNEYNGSYVPPGWKEWVGLLKNSRFYNYTLCRNGVKEKHGSD  
YSKDYLTDLITNDSVSFFRTSKKMPHRPVLVISHAAPHGPEDSAPQYSRLFPNASQHITP  
SYNYAPNPDKHWIMRYTGPMKPIHMEFTNMLQQRKLQTLMSVDDSMETIYNMLVETGELDNT  
YIVYTADHGYHIGQFGLVKGKSMPEFDIRVFFYVRGPNVEAGCLNPHIVLNIDLAPTILDI  
AGLDIPADMKGKSLKLLDTERPVNRFHLKKKMRVWRDSFLVERGKLLHKRDNDKVDAQEEN  
FLPKYQRVKDLQRAEYQTACEQLGQKWQCVEDATGKLKHLKCKGPMRLGGSRALSNLVPKY  
YGQGSEACTCDSDYKLSLAGRRKKLFKKKYKASYVRSRSIRSVAI EVDGRVYHVGLGDAAQ  
PRNLTKRHWP GAPEDQDDKDGGDFSGTGGLPDYSAANPIKVTHRCYILENDTVQCDLDLYKS  
LQAWKDHKLHIDHEIETLQNKIKNLREVRGHLKKKRPEECDCHKISYHTQHKGRLKHRGSSL  
HPFRKGLQEKDKVWLLREQKRKKLRKLLKRLQNNDTCSMPGLTCFTHDNQHWQTAPFWTLG  
PFCACTSANNNTYWC MRTINETHNFLFCEFATGFLEYFDLNTDPYQLMNAVNTLDRDVLNQL  
HVQLMELRSCKGYKQCNPRTRNMDLDGGSYEQYRQFQRRKWPEMKRPSSKSLGQLWEGWEG

48/330

**FIGURE 48**

AACAAAGTTCAGTGA CTGAGAGGGCTGAGCGGAGGCTGCTGAAGGGGAGAAAGGAGTGAGGA  
GCTGCTGGGCAGAGAGGGACTGTCCGGCTCCCAG**ATG**CTGGGCCTCCTGGGGAGCACAGCCC  
TCGTGGGATGGATCACAGGTGCTGCTGTGGCGGTCCTGCTGCTGCTGCTGCTGCTGGCCACC  
TGCCTTTTCCACGGACGGCAGGACTGTGACGTGGAGAGGAACCGTACAGCTGCAGGGGGAAA  
CCGAGTCCGCCGGGCCCCAGCCTTGGCCCTTCCGGCGGGCGGGGCCACCTGGGAATCTTTCACC  
ATCACCGTCATCCTGGCCACGTATCTCATGTGCCGAATGTGGGCCTCCACCACCACCACCAC  
CCCCGCCACACCCCTCACCACCTCCACCACCACCACCACCCCCACCGCCACCATCCCCGCCA  
CGCTCGC**TGA**GGCTGCTGTGCGCCGGTGCCTGTGGACAGCAGCTGCCCCCTGCCCTCCCATCTG  
TCCCAGGACAAGTGGACCCCATGTTTCCATGTGGAAGGATGCATCTCTGGGGTGAACGAGG  
GGAACAATAGACTGGGGCTTGCTCCAGCTGCATTTGCATGGCATGCCCCAGTGTACTATGGC  
AGCAGAGAATGGAGGAACACTGGGTCTGCAGTGCTGAAGGGTTTGGGGAGTGGAGAGCAAGG  
GTGCTCTTTCGGGGCTGGACAGCCCGTCTTG TGACAGTGACTCCCAGTGAGCCCCAGAAATG  
ACAAGCGTGTCTTGGCAGAGCCAGCACACAAGTGGATGTGAAGTGCCCGTCTTGACCTCCTC  
ATCAGGCTGCTGCAGGCCTCTGGCGGGCAGGGCACTGGGAGAGGCCCTGAGAATGTCCTTTT  
GGTTTGGAGAAGGCAGTGTGAGGCTGCACAGTCAATTCATCGGTGCCTTAGTCCAAGAAAAT  
AAAAACCACTAAGAAGCTTTAAAAAAAAAAAAAAAAAAAAA

49/330

**FIGURE 49**

MLGLLGSTALVGWITGAAVAVLLLLLLLLLATCLFHGRQDCDVERNRTAAGGNRVRRAQPWPFRR  
RRGHLGIFHHHRHPGHVSHVPNVGLHHHHHPRHTPHHLHHHHHPRHHPRHAR

50/330

**FIGURE 50**

GGCGGCTGCTGAGCTGCCTTGAGGTGCAGTGTTGGGGATCCAGAGCC**ATG**TCGGACCTGCTA  
CTACTGGGCCTGATTGGGGGCCTGACTCTCTTACTGCTGCTGACGCTGCTGGCCTTTGCCGG  
GTACTCAGGGCTACTGGCTGGGGTGGAAAGTGAGTGCTGGGTACCCCCCATCCGCAACGTCA  
CTGTGGCCTACAAGTTCCACATGGGGCTCTATGGTGAGACTGGGCGGCTTTTCACTGAGAGC  
TGCAGCATCTCTCCCAAGCTCCGCTCCATCGCTGTCTACTATGACAACCCCCACATGGTGCC  
CCCTGATAAGTGCCGATGTGCCGTGGGCAGCATCCTGAGTGAAGGTGAGGAATCGCCCTCCC  
CTGAGCTCATCGACCTCTACCAGAAATTTGGCTTCAAGGTGTTCTCCTTCCCGGCACCCAGC  
CATGTGGTGACAGCCACCTTCCCCTACACCACCATTTCTGTCCATCTGGCTGGCTACCCGCCG  
TGTCCATCCTGCCTTGGACACCTACATCAAGGAGCGGAAGCTGTGTGCCTATCCTCGGCTGG  
AGATCTACCAGGAAGACCAGATCCATTTTCATGTGCCCACTGGCACGGCAGGGAGACTTCTAT  
GTGCCTGAGATGAAGGAGACAGAGTGGAATGGCGGGGGCTTGTGGAGGCCATTGACACCCA  
GGTGGATGGCACAGGAGCTGACACAATGAGTGACACGAGTTCTGTAAGCTTGGAAGTGAGCC  
CTGGCAGCCGGGAGACTTCAGCTGCCACACTGTCACCTGGGGCGAGCAGCCGTGGCTGGGAT  
GACGGTGACACCCGCAGCGAGCACAGCTACAGCGAGTCAGGTGCCAGCGGCTCCTCTTTTGA  
GGAGCTGGACTTGGAGGGCGAGGGGCCCTTAGGGGAGTCACGGCTGGACCCTGGGACTGAGC  
CCCTGGGGACTACCAAGTGGCTCTGGGAGCCCACTGCCCCTGAGAAGGGCAAGGAG**TAA**CCC  
ATGGCCTGCACCCTCCTGCAGTGCAGTTGCTGAGGAACTGAGCAGACTCTCCAGCAGACTCT  
CCAGCCCTCTTCCTCCTTCCTCTGGGGGAGGAGGGGTTCTGAGGGACCTGACTTCCCCTGC  
TCCAGGCCTCTTGCTAAGCCTTCTCCTCACTGCCCTTTAGGCTCCCAGGGCCAGAGGAGCCA  
GGGACTATTTTCTGCACCAGCCCCCAGGGCTGCCGCCCTGTTGTGTCTTTTTTTTCACTC  
ACAGTGGAGCTTCCAGGACCCAGAATAAAGCCAATGATTTACTTGTTTCACCTGGAAAAAA  
AAAAA

51/330

**FIGURE 51**

MSDLLLLGLIGGLTLLLLLTLLAFAGYSGLLAGVEVSAGSPPIRNVTVAYKFHMGlyGETGR  
LFTESCSISPKLRsIAVYYDNPHMVPPDKCRAVGsILSEGEESPSPELIDLYQKFGFKVFS  
FPAPSHVVTATFPYTTILSIWLATRRVHPALDTYIKERKLCAYPRLEIYQEDQIHfMCPLAR  
QGDFYVPEMKETEWKWRGLVEAIDTQVDGTGADTMSDTSSVSLEVSPGSRETSAATLSPGAS  
SRGWDDGDTRSEHSYSESGASGSSFEELDLEGEGLGESRLDPGTEPLGTTKWLWEPTAPEK  
GKE



52/330

**FIGURE 52**

CCGCGGGAACGCTGTCCTGGCTGCCGCCACCCGAACAGCCTGTCCTGGTGCCCCGGCTCCCT  
GCCCCGCGCCCAGTC**ATG**ACCCTGCGCCCCCTCACTCCTCCCGCTCCATCTGCTGCTGCTGCT  
GCTGCTCAGTGCGGCGGTGTGCCGGGCTGAGGCTGGGCTCGAAACCGAAAGTCCCGTCCGGA  
CCCTCCAAGTGGAGACCCTGGTGGAGCCCCCAGAACCATGTGCCGAGCCCGCTGCTTTTGA  
GACACGCTTCACATACACTACACGGGAAGCTTGGTAGATGGACGTATTATTGACACCTCCCT  
GACCAGAGACCCTCTGGTTATAGAACTTGGCCAAAAGCAGGTGATTCCAGGTCTGGAGCAGA  
GTCTTCTCGACATGTGTGTGGGAGAGAAGCGAAGGGCAATCATTCTTCTCACTTGGCCTAT  
GGAAAACGGGGATTTCCACCATCTGTCCCAGCGGATGCAGTGGTGCAGTATGACGTGGAGCT  
GATTGCACTAATCCGAGCCAACTACTGGCTAAAGCTGGTGAAGGGCATTTTGCCTCTGGTAG  
GGATGGCCATGGTGCCAGCCCTCCTGGGCCTCATTGGGTATCACCTATACAGAAAGGCCAAT  
AGACCCAAAGTCTCCAAAAAGAAGCTCAAGGAAGAGAAACGAAACAAGAGCAAAAAGAA**TA**  
**A**TAAATAATAAATTTTAAAAAACTTAAAAAAAAAAAAAAAAAAAA

53/330

**FIGURE 53**

MTLRPSLLPLHLLLLLLLLSAAVCRAEAGLETESPVRTLQVETLVEPPEPCAEPAAFGLTLHI  
HYTGSLVDGRIIDTSLTRDPLVIELGQKQVIPGLEQSLLDMCVGEKRRATIPSHLAYGKRGF  
PPSVPADAVVQYDVELIALIRANYWLKLVKGILPLVGMAMVPALLGLIGYHLYRKANRPKVS  
KKKLKEEKRNKSKKK

54/330

**FIGURE 54**

CCCGGGAACGTGTTCTGGCTGCCGCACCCGAACAGCCTGTCCTGGTGCCCCGGCTCCCTGC  
CCCGCGCCCAGTCATGACCCTGCGCCCCTCACTCCTCCCGCTCCATCTGCTGCTGCTGCTGC  
TGCTCAGTGCGGCGGTGTGCCGGGCTGAGGCTGGGCTCGAAACCGAAAGTCCCGTCCGGACC  
CTCCAAGTGGAGACCCTGGTGGAGCCCCCAGAACCATGTGCCGAGCCCGCTGCTTTTGGAGA  
CACGCTTCACATACTACACGGGAAGCTTGGTAGATGGACGTATTATTGACACCTCCCTGA  
CCAGAGACCCTCTGGTTATAGAACTTGGCCAAAAGCAGGTGATTCCAGGTCTGGAGCAGAGT  
CTTCTCGACATGTGTGTGGGAGAGAAGCGAAGGGCAATCATTCTTCTCACTTGGCCTATGG  
AAAACGGGGATTTCCACCATCTGTCCCAGCGGATGCAGTGGTGCAGTATGACGTGGAGCTGA  
TTGCACTAATCCGAGCCAACCTACTGGCTAAAGCTGGTGAAGGGCATTTTGCCTCTGGTAGGG  
ATGGCCATGGTGCCACCCTCCTGGGCCTCATTGGGTATCACCTATACAGAAAGGCCAATAGA  
CCCAAAGTCTCCAAAAAGAAGCTCAAGGAAGAGAAACGAAACAAGAGCAAAAAGAAATAATA  
AATAATAAATTTTAAAAAACTTA

55/330

**FIGURE 55**

CCGAAAGTCCCGTCCGGACCCTCCAAGTGGAGACCCTGGTGGAGCCCCCAGAACCATGTGCC  
GAGCCCGCTGCTTTTGGAGACACGCTTCACATACACTACACGGGAAGCTTGGTAGATGGACG  
TATTATTGACACCTCCCTGACCAGAGACCCTCTGGTTATAGAAGTTGGCCAAAAGCAGGTGA  
TTCCAGGTCTGGAGCAGAGTCTTCTCGACATGTGTGTGGGAGAGAAGCGAAGGGCAATCATT  
CCTTCTCACTTGGCCTATGGAAAACGGGGATTTCCACCATCTGTCCCAGCGGATGCAGTGGT  
GCAGTATGACGTGGAGCTGATTGCACTAATCCGAGCCAACACTGGCTAAAGCTGGTGAAGG  
GCATTTTGCCTCTGGTAGGGATGGCCATGGTGCCAGCCCTCCTGGGCCTCATTGGGTATCAC  
CTATACAGAAAGGCCAATAGACCCAAAGTCTCCAAAAGAAGCTCAAGGAAGAGAAACGAAA  
CAAGAGCAAAAAGAAATAATAAATAATAAATTTTAAAAAACTTAAAA

56/330

**FIGURE 56**

CTGCTGCATCCGGGTGTCTGGAGGCTGTGGCCGTTTTGTTTTCTTGGCTAAAATCGGGGGAG  
TGAGGCGGGCCGGCGCGGCGGACACCGGGCTCCGGAACCACTGCACGACGGGGCTGGACTG  
ACCTGAAAAAA**ATG**CTGGATTTCTAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGG  
GAAAAGCGCAATACTATTGCTTCCATTGCTGCTGGTGTACTATTTTTTACAGGCTGGTGGAT  
TATCATAGATGCAGCTGTTATTTATCCACCATGAAAGATTTCAACCACTCATACCATGCCT  
GTGGTGTATAGCAACCATAGCCTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGA  
GGTGATAGTTACAGTGAAGTTGTCTGGGTCAAACAGGTGCTCGCATTTGGCTTTTCGTTGG  
TTTCATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGGATTCTTTTTGGAGGTTATGTTG  
CTAAAGAAAAAGACATAGTATACCCTGGAATTGCTGTATTTTTCCAGAATGCCTTCATCTTT  
TTTGGAGGGCTGGTTTTTAAGTTTGGCCGCACTGAAGACTTATGGCAG**TGA**ACACATCTGAT  
TTCCACAGCACAACAGCCCTGCATGGGTTTGTGTTTTTTTTACTGCTCACTCCCAACCTT  
TTGTAATGCCATTTTCTAACTTATTTCTGAGTGTAGTCTCAGCTTAAAGTTGTGTAATACT  
AAAATCACGAGAACACCTAAACAACAACCAAAAATCTATTGTGGTATGCACTTGATTAACCT  
ATAAAATGTTAGAGGAACTTTCACATGAATAATTTTTGTCAAATTTTATCATGGTATAATT  
TGTA AAAAATAAAAAGAAATTACAAAAGAAATTATGGATTTGTCAATGTAAGTATTTGTCATA  
TCTGAGGTCCAAAACCACAATGAAAGTGCTCTGAAGATTTAATGTGTTTATTCAAATGTGGT  
CTCTTCTGTGTCAAATGTTAAATGAAATATAAACATTTTTTAGTTTTTAAATATTCCGTGG  
TCAAAATTCTTCCTCACTATAATTGGTATTTACTTTTACCAAAAATTCTGTGAACATGTAAT  
GTAAC TGGCTTTTGAGGGTCTCCCAAGGGGTGAGTGGACGTGTTGGAAGAGAGAAGCACCAT  
GGTCCAGCCACCAGGCTCCCTGTGTCCCTTCCATGGGAAGGTCTTCCGCTGTGCCTCTCATT  
CCAAGGGCAGGAAGATGTGACTCAGCCATGACACGTGGTCTGGTGGGATGCACAGTCACTC  
CACATCCACCACTG

57/330

**FIGURE 57**

MSGFLEGLRCSECIDWGEKRNTIASIAAGVLFFTGWIIIDAAVIYPTMKDFNHSYHACGVI  
ATIAFLMINAVSNGQVRGDSYSEGCLGQTGARIWLFVGFMLAFGSLIASMWILFGGYVAKEK  
DIVYPGIAVFFQNAFIFFGGLVFKFGRTEDLWQ

58/330

**FIGURE 58**

TTCTTGGCTAAAATCGGGGGAGTGAGGCGGGCCGGCGCGGCACACCGGGCTCCGGAACC  
ACTGCACGACGGGGCTGGACTGACCTGAAAAAATGTCTGGATTTCTAGAGGGCTTGAGATG  
CTCAGAATGCATTGACTGGGGGGAAAAGCGCAATACTATTGCTTCCATTGCTGCTGGTGTAC  
TATTTTTTTACAGGCTGGTGGATTATCATAGATGCAGCTGTTATTTATCCCACCATGAAAGAT  
TTCAACCACTCATAACCATGCCTGTGGTGTATAGCAACCATAGCCTTCCTAATGATTAATGC  
AGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTTGTCTGGGTCAAACAGGTG  
CTCGCATTTGGCTTTTCGTTGGTTTCATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGG  
ATTCTTTTTTGGAGGTTATGTTGCTAAAGAAAAAGACATAGTATACCCTGGAATTGCTGTATT  
TTTCCAGAATGCCTTCATCTTTTTTTGGAGGGCTGGTTTTTTAAGTTTGGC

59/330

**FIGURE 59**

TGGACGGACCTGAAAAAATGTTTGGATTTNTAGAGGGNTTGAGATGTTTCAGAATGCATGAC  
TGGGGGAAAAGCGCAAATACTATTGCTTCCATTGCTGCTGGTGTANTATTTTTTACAGGCTG  
GTGGATTATCATAGATGCAGNTGTTATTTATCCCACCATGAAAGATTTCAACCANTCATACC  
ATGCCTGTGGTGTTATAGCAACCATAGCCTTCNTAATGATTAATGCAGTATCGAATGGACAA  
GTCCGAGGTGATAGTTACAGTGAAGGTTGTTTGGGTCAAACAGGTGCTCGCATTTGGCTTTT  
CGTTGGTTTCATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGGATTCTTTTTGGAGGTT  
ATGTTGCTAAAGAAAAAGACATAGTATAACCCTGGAATTGNTGTATTTTTCCAGAATGCCTTC  
ATCTTTTTTGGAGGGCTGGTTTTTAAGTTTGGCCGCACTGAAGANTTATGGCAGTG



60/330

**FIGURE 60**

GGACACCGGGTTCCGGACCAATGCANGACGGGGTGGANTGACCTGAAAAAATGTTTGGATT  
TTTAGAGGGCTTGAGATGNTCAGAATGCATTGACTGGGGGAAAAGCGCAATANTATTGCTTT  
CCATTGCTGCTGGTGTACTATTTTTTACAGGGTGGTGGATTATCATAGATGCAGCTGTTATT  
TATCCCACCATGAAAGATTTNAACCACTCATACCATGCCTGTGGTGTATAGCAACCATAGC  
CTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTT  
GTTTGGGTCAAACAGGTGNTCGCATTTGGCTTTTCGTTGGTTTCATGTTGGCCTTTGGATTT  
CTGATTGNATTCTATGCGGATTCTTCTTGGAGGTTATGTTGCTAAAGAAAAGACATAGTAT  
ACCCTGGAATTNCTNTATTTTTTCCAGAATGCC

61/330

**FIGURE 61**

TAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGGGAAAAGCGCAATANTATTGCTTCC  
ATTGNTGNTGGTGTANTATTTTTTTTACAGGCTGGTGGATTATNATAGATGCAGCTGTTATTT  
ATCCCACCATGAAAGATTTNAACCANTCATACCATGCCTGTGGTGTTATAGCAACCATAGCC  
TTCCTAATGATTAATGCAGTATNGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTTG  
TTTGGGTCAAACAGGTGNTNGCATTTGGCTTTTNGTTGGTTTCATGTTGGCCTTTGGATCTN  
TGATTGCATTTATGTGGATTNTTTTTTGGAGGTTATGTTGCTAAAGNAAAAGACATAGTATAC  
CCTGT

62/330

**FIGURE 62**

GGGAGGCTGTGNCCGTTTTGTTTTNTTGGCTAAAATCGGGGGAGTGAGGCGGCCCGGCGCGG  
CGNGACACCGGGTTCCGGGAACCATTCACGACGGGGTGGACTGACCTGAAAAAATGTTTG  
GATTTNTAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGGGAAAAGCGCAATACTATT  
GCTTCCATTGCTGCTGGTGTACTATTTTTTACAGGCTGGTGGATTATCATAGATGCAGCTGT  
TATTTATCCCACCATGAAAGATTTCAACCACTCATACCATGCCTGTGGTGTTATAGCAACCA  
TAGCCTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAA  
GGTTGTCTGGGTCAAACAGGTGCTCGCATTGCGCTTTTCGTTGGTTTCATGTTGGCCTTTGG  
ATNTCTGATTGCATCTATGTGGATTCTTTTTGGAGGTTATGTTGCTAAAGAAAAAGACATAG  
TATACCCTGGAATTGCTGTATTTTTCCAGAATGCCTTCATNTTTTTTTGGAGGGCTG

63/330

**FIGURE 63**

CGACGCCGGCGTG**ATG**TGGCTTCCGCTGGTGTGCTGCTCCTGGCTGTGCTGCTGCTGGCCGTCC  
TCTGCAAAGTTTACTTGGGACTATTCTCTGGCAGCTCCCCGAATCCTTTCTCCGAAGATGTC  
AAACGGCCCCCAGCGCCCCCTGGTAACTGACAAGGAGGCCAGGAAGAAGGTTCTCAAACAAGC  
TTTTTTCAGCCAACCAAGTGCCGGAGAAAGCTGGATGTGGTGGTAATTGGCAGTGGCTTTGGGG  
GCCTGGCTGCAGCTGCAATTCTAGCTAAAGCTGGCAAGCGAGTCCTGGTGTGGAACAACAT  
ACCAAGGCAGGGGGGCTGCTGTCATACCTTTGGAAAGAATGGCCTTGAATTTGACACAGGAAT  
CCATTACATTGGGCGTATGGAAGAGGGCAGCATTGGCCGTTTTATCTTGGACCAGATCACTG  
AAGGGCAGCTGGACTGGGCTCCCCTGTCTCTCTCTTTTGGACATCATGGTACTGGAAGGGCCC  
AATGGCCGAAAGGAGTACCCCATGTACAGTGGAGAGAAAAGCCTACATTACAGGGCCTCAAGGA  
GAAGTTTCCACAGGAGGAAGCTATCATTGACAAGTATATAAAGCTGGTTAAGGTGGTATCCA  
GTGGAGCCCCCTCATGCCATCCTGTTGAAATTCCTCCCATTGCCCGTGGTTTACAGCTCCTCGAC  
AGGTGTGGGCTGCTGACTCGTTTCTCTCCATTCTTCAAGCATCCACCCAGAGCCTGGCTGA  
GGTCTCTGCAGCAGCTGGGGGCTCCTCTGAGCTCCAGGCAGTACTCAGCTACATCTTCCCCA  
CTTACGGTGTCAACCCCAACACAGTGCCTTTTTCCATTGCACGCCCTGCTGGTCAACCACTAC  
ATGAAAGGAGGCTTTTTATCCCCGAGGGGGTTCCAGTGAAATTGCCTTCCACACCATCCCTGT  
GATTACAGCGGGCTGGGGGCGCTGTCTCACAAAGGCCACTGTGCAGAGTGTGTTGCTGGACT  
CAGCTGGGAAAGCCTGTGGTGTGAGTGTGAAGAAGGGGCATGAGCTGGTGAACATCTATTGC  
CCCATCGTGGTCTCCAACGCAGGACTGTTCAACACCTATGAACACCTACTGCCGGGGAACGC  
CCGCTGCCTGCCAGGTGTGAAGCAGCAACTGGGGACGGTGCAGGCGGGCTTAGGCATGACCT  
CTGTTTTTCTGCTGCGAGGCACCAAGGAAGACCTGCATCTGCCGTCCACCAACTACTAT  
GTTTACTATGACACGGACATGGACCAGGCGATGGAGCGCTACGTCTCCATGCCCAGGGAAGA  
GGCTGCGGAACACATCCCCCTTCTCTTCTTCTCGCTTTCCCATCAGCCAAAGATCCGACCTGGG  
AGGACCGATTCCCAGGCGGTCCACCATGATCATGCTCATACCCACTGCCTACGAGTGGTTT  
GAGGAGTGGCAGGCGGAGCTGAAGGGAAAGCGGGCAGTGACTATGAGACCTTCAAAAATC  
CTTTGTGGAAGCCTCTATGTGAGTGGTCTGAAACTGTTCCACAGCTGGAGGGGAAGGTGG  
AGAGTGTGACTGCAGGATCCCCACTCACCACCAAGTCTATCTGGCTGCTCCCCGAGGTGCC  
TGCTACGGGGCTGACCATGACCTGGGCGCCTGCACCCCTTGTGTGATGGCCTCCTTGAGGGC  
CCAGAGCCCCATCCCCAACCTCTATCTGACAGGCGAGGATATCTTCACTGTGAGTGGTGG  
GGCCCTGCAAGGTGCCCTGCTGTGCAGCAGCGCCATCCTGAAGCGGAACCTGTACTCGAC  
CTTAAGAATCTTGATTCTAGGATCCGGGACAGAAAGAAAAGAAT**TAG**TTCCATCAGGGAGG  
AGTCAGAGGAATTTGCCCAATGGCTGGGGCATCTCCCTTGACTTACCCATAATGTCTTTCTG  
CATTAGTTCTTGCACGTATAAAGCACTCTAATTTGGTTCTGATGCCTGAAGAGAGGCCTAG  
TTTAAATCACAATTCCGAATCTGGGGCAATGGAATCACTGCTTCCAGCTGGGGCAGGTGAGA  
TCTTTTACGCCTTTTATAACATGCCATCCCTACTAATAGGATATTGACTTGGATAGCTTGATG  
TCTCATGACGAGCGGCGCTCTGCATCCCTCACCCATGCCCTCCTAACTCAGTGATCAAAGCGA  
ATATTCCATCTGTGGATAGAACCCTGGCAGTGTGTGAGCTCAACCTGGTGGGTTGAGTTC  
TGTCCTGAGGCTTCTGCTCTCATTCATTTAGTGCTACGCTGCACAGTTCTACACTGTCAAGG  
GAAAAGGGAGACTAATGAGGCTTAACTCAAAACCTGGGCGTGGTTTTGGTTGCCATTCCATA  
GGTTTTGGAGAGCTCTAGATCTCTTTTGTGCTGGGTTTCACTGGCTCTTCAGGGGACAGGAAAT  
GCCTGTGTCTGGCCAGTGTGGTTCTGGAGCTTTGGGGTAACAGCAGGATCCATCAGTTAGTA  
GGGTGCATGTGAGATGATCATATCCAATTCATATGGAAGTCCCGGGTCTGTCTTCTTATCA  
TCGGGGTGGCAGCTGGTTCTCAATGTGCCAGCAGGGACTCAGTACCTGAGCCTCAATCAAGC  
CTTATCCACCAAATACACAGGGAAGGGTGTGTCAGGGAAGGGTGACATCAGGAGTCAGGGCA  
TGGACTGGTAAGATGAATACTTTGCTGGGCTGAAGCAGGCTGCAGGGCATTCCAGCCAAGGG  
CACAGCAGGGGACAGTGCAGGGAGGTGTGGGGTAAGGGAGGGAAGTCACATCAGAAAAGGGA  
AAGCCACGGAATGTGTGTGAAGCCCAGAAATGGCATTTGCAGTTAATTAGCACATGTGAGGG  
TTAGACAGGTAGGTGAATGCAAGCTCAAGGTTTGGAAAAATGACTTTTCAGTTATGTCTTTG  
GTATCAGACATACGAAAGGTCTCTTTGTAGTTTCGTGTTAATGTAACATTAATAAATTTATTG  
ATTCCATTGCTTTAAAAA

64/330

**FIGURE 64**

MWLPLVLLLLAVLLLLAVLCKVYLGLFSGSSPNPFSEDEVKRPPAPLVTDKEARKKVLKQAFSAN  
QVPEKLDVVVIGSGFGGLAAAAILAKAGKRVLVLEQHTKAGGCCHTFGKNGLEFDTGIHYIG  
RMEEGSIGRFILDQITEGQLDWAPLSSPFDIMVLEGPNGRKEYPMYSGEKAYIQGLKEKFPQ  
EEAIIIDKYIKLVKVSSGAPHAILLKFLPLPVVQLLDRCGLLTRFSPFLQASTQSLAEVLQQ  
LGASSELQAVLSYIFPTYGVTPNHSAFSMHALLVNHYMKGGFYPRGGSSEIAFHTIPVIQRA  
GGAVLTKATVQSVLLDSAGKACGVSVKKGHELVNIYCPIVVSNAGLFNTYEHLLPGNARCLP  
GVKQQLGTVRPGLGMTSVFICLRGTKEDLHLPSTNYVYVYDMDQAMERYVSMPREEAAEH  
IPLFFFAFPSAKDPTWEDRFPGRSTMIMLIPTAYEWFEWQAELKGKRGSDYETFKNSFVEA  
SMSVVLKLFQLEGKVESVTAGSPLTNQFYLAAPRGACYGADHDLGRLHPCVMASLRAQSPI  
PNLYLTGQDIFTCGLVGALQGALLCSSAILKRNLYSDLKNLDSRIRAQKKKN

65/330

**FIGURE 65**

[illegible]

66/330

**FIGURE 66**

MRVRIGLTLLLCVLLSLASASSDEEGSQDES LDSKTTLTSDSVKDHTTAGRVVAGQIFLD  
SESELESSIQEEEDSLKSQEGESVTEDISFLESPNPENKDYEEP KVKVRKPALTAIEGTAHG  
EPCHF PFLFLDKEYDECTSDGREDGRLWCATTYDYKADEKWGFCETEEEAARRQM QEAEMM  
YQTGMKILNGSNKKSQKREAYRYLQKAASMNHTKALERVSYALLFGDYLPQNIQAAREMF EK  
LTEEGSPKGQTALGFLYASGLGVNSSQAKALVYYTFGALGGNLI AHMVLVSRL

67/330

**FIGURE 67**

CTTCCCAGCCCTGTGCCCCAAAGCACCTGGAGCATATAGCCTTGCAGAACTTCTACTTGCCT  
GCCTCCCTGCCTCTGGCC**ATG**GCCTGCCGGTGCCTCAGCTTCCTTCTGATGGGGACCTTCCT  
GTCAGTTTCCCAGACAGTCCTGGCCCAGCTGGATGCACTGCTGGTCTTCCCAGGCCAAGTGG  
CTCAACTCTCCTGCACGCTCAGCCCCCAGCACGTCACCATCAGGGACTACGGTGTGTCCTGG  
TACCAGCAGCGGGCAGGCAGTGGCCCTCGATATCTCCTCTACTACCGCTCGGAGGAGGATCA  
CCACCGGCCTGCTGACATCCCCGATCGATTCTCGGCAGCCAAGGATGAGGCCCAACAATGCCT  
GTGTCCTCACCATTAGTCCCGTGCAGCCTGAAGACGACGCGGATTACTACTGCTCTGTTGGC  
TACGGCTTTAGTCCC**TAG**GGGTGGGGTGTGAGATGGGTGCCTCCCCTCTGCCTCCCATTTCT  
GCCCCTGACCTTGGGTCCCTTTTAAACTTTCTCTGAGCCTTGCTTCCCCTCTGTAAAATGGG  
TTAATAATATTCAACATGTCAACAAC



68/330

**FIGURE 68**

MACRCLSFLMGTFLSVSQTVLAQLDALLVFPQVAQLSCTLSPQHVTIRDYGVSWYQQRAG  
SAPRYLLYYRSEEDHHRPADIPDRFSAKDEAHNACVLTISPVPEDDADYYCSVGYGFSF

69/330

**FIGURE 69**

GCCGCCCCGCCCGAGACCGGGCCCCGGGGGCGCGGGGCGGCGGGGATGCGGCGCCCCGGGGCGG  
CGATGACCGCGGGAGCGCACGCCGCGGGGCCCGGCCCTGACCCCGCCGCCCGCCCCGCTGAGCCC  
CCCCCGGAGGTCCGGACAGGCCGAG**ATG**ACGCCGAGCCCCCTGTTGCTGCTCCTGCTGCCGC  
CGCTGCTGCTGGGGGCCCTTCCCACCGGCCGCCGCCGCCGAGGCCCCCCAAAGATGGCGGAC  
AAGGTGGTCCCACGGCAGGTGGCCCGGCTGGGCGGCACTGTGCGGCTGCAGTGCCCAAGTGA  
GGGGGACCCGCCGCCGCTGACCATGTGGACCAAGGATGGCCGCACCATCCACAGCGGCTGGA  
GCCGCTTCCGCGTGCTGCCGCAGGGGCTGAAGGTGAAGCAGGTGGAGCGGGAGGATGCCGGC  
GTGTACGTGTGCAAGGCCACCAACGGCTTCGGCAGCCTGAGCGTCAACTACACCCCTCGTCGT  
GCTGGATGACATTAGCCCAGGGAAGGAGAGCCTGGGGCCCCGACAGCTCCTCTGGGGGTCAAG  
AGGACCCCGCCAGCCAGCAGTGGGCACGACCGCGCTTCACACAGCCCTCCAAGATGAGGCGC  
CGGGTGATCGCACGGCCCCGTGGGTAGCTCCGTGCGGCTCAAGTGCGTGGCCAGCGGGCACCC  
TCGGCCCCGACATCACGTGGATGAAGGACGACCAGGCCTTGACGCGCCCAGAGGCCGCTGAGC  
CCAGGAAGAAGAAGTGGACACTGAGCCTGAAGAACCTGCGGCCGGAGGACAGCGGCAAATAC  
ACCTGCCGCGTGTCGAACCGCGCGGCGCCATCAACGCCACCTACAAGGTGGATGTGATCCA  
GCGGACCCGTTCCAAGCCCGTGCTCACAGGCACGCACCCCGTGAACACGACGGTGGACTTCG  
GGGGGACCACGTCCTTCCAGTGCAAGGTGCGCAGCGACGTGAAGCCGGTGATCCAGTGGCTG  
AAGCGCGTGAGTACGGCGCCGAGGGCCGCCACAACCTCCACCATCGATGTGGGCGGCCAGAA  
GTTTGTGGTGCTGCCACGGGTGACGTGTGGTTCGCGGCCCGACGGCTCCTACCTCAATAAGC  
TGCTCATCACCCGTGCCCGCCAGGACGATGCGGGCATGTACATCTGCCTTGGCGCCAAACAC  
ATGGGCTACAGCTTCCGCAGCGCCTTCCTCACCGTGCTGCCAGACCCAAAACCGCCAGGGCC  
ACCTGTGGCCTCCTCGTCCTCGGCCACTAGCCTGCCGTGGCCCGTGCTCATCGGCATCCAG  
CCGGCGCTGTCTTCATCCTGGGCACCCTGCTCCTGTGGCTTTGCCAGGCCCAGAAGAAGCCG  
TGACCCCCCGCGCTGCCCTCCCCCTGCCTGGGCACCGCCCGCCGGGGACGGCCCCGCGACC  
CAGCGGAGACAAGGACCTTCCCTCGTTGGCCGCCCTCAGCGCTGGCCCTGGGTGTGGGCTGT  
GTGAGGAGCATGGGTCTCCGGCAGCCCCCAGCACTTACTGGGCCCAGGCCCAGTTGCTGGC  
CCTAAGTTGTACCCCAAACCTCTACACAGACATCCACACACACACACACACACTCTCACAC  
ACACTCACACGTGGAGGGCAAGGTCCACCAGCACATCCACTATCAGTGCT**TAG**ACGGCACCGT  
ATCTGCAGTGGGCACGGGGGGGCCCGCCAGACAGGCAGACTGGGAGGATGGAGGACGGAGCT  
GCAGACGAAGGCAGGGGACCCATGGCGAGGAGGAATGGCCAGCACCCAGGCAGTCTGTGTG  
TGAGGCATAGCCCCCTGGACACACACACACAGACACACACACTACCTGGATGCATGTATGCAC  
ACACATGCGCGCACACGTGCTCCCTGAAGGCACACGTACGCACACGCACATGCACAGATATG  
CCGCCTGGGCACACAGATAAGCTGCCCAAATGCACGCACACGCACAGAGACATGCCAGAACA  
TACAAGGACATGCTGCCTGAACATAACACGCACACCCATGCGCAGATGTGCTGCCTGGACA  
CACACACACACACGATATGCTGTCTGGACGCACACACGTGCAGATATGGTATCCGGACACA  
CACGTGCACAGATATGCTGCCTGGACACACAGATAATGCTGCCTTGACACACACATGCACGG  
ATATTGCCTGGACACACACACACACACACGCGTGACAGATATGCTGTCTGGACACGCACAC  
ACATGCAGATATGCTGCCTGGACACACACTTCCAGACACACGTGCACAGGCGCAGATATGCT  
GCCTGGACACACGCAGATATGCTGTCTAGTCACACACACACGCAGACATGCTGTCCGGACAC  
ACACACGCATGCACAGATATGCTGTCCGGACACACACACGCACGCAGATATGCTGCCTGGAC  
ACACACACAGATAATGCTGCCTCAACACTCACACACGTGCAGATATTGCCTGGACACACACA  
TGTGCACAGATATGCTGTCTGGACATGCACACACGTGCAGATATGCTGTCCGGATACACACG  
CACGCACACATGCAGATATGCTGCCTGGGCACACACTTCCGGACACACATGCACACACAGGT  
GCAGATATGCTGCCTGGACACACACAGATAATGCTGCCTCAACACTCACACACGTGCAGATA  
TATTGCCTGGACACACACATGTGCACAGATATGCTGTCTGGACATGCACACACGTGCAGATA  
TGCTGTCCGGATACACACGCACGCACACATGCAGATATGCTGCCTGGGCACACACTTCCGGA  
CACACATGCACACACAGGTGCAGATATGCTGCCTGGACACACGCAGACTGACGTGCTTTTGG  
GAGGGTGTGCCGTGAAGCCTGCAGTACGTGTGCCGTGAGGCTCATAGTTGATGAGGGACTTT  
CCTTGCTCCACCGTCACTCCCCAACTCTGCCCGCCTCTGTCCCCGCCTCAGTCCCCGCCTC  
CATCCCCGCCTGTGTCCCCTGGCCTTGGCGCTGCTATTTTGGCACCTGCCTTGGGTGCCCAGG  
AGTCCCCTACTGCTGTGGGCTGGGGTTGGGGGCACAGCAGCCCCAAGCCTGAGAGGCTGGAG  
CCCATGGCTAGTGGCTCATCCCCAGTGCATTCTCCCCCTGACACAGAGAAGGGGCCTTGGTA  
TTTATATTTAAGAAATGAAGATAATATTAATAATGATGGAAGGAAGACTGGGTTGCAGGGAC  
TGTTGGTCTCTCCTGGGGCCCCGGGACCCGCTGGTCTTTTACGCCATGCTGATGACCAACCCCC  
GTCCAGGCCAGACACACACCCCGCTGTGCTGGTGGTGGCCCCAGATCTGTGAATTTTA  
TGTAAGATTTGAGCTGAAGCCCCGTATATTTAATTTATTTTGTAAACACAAAA

70/330

**FIGURE 70**

MTPSPLLLLLLLPPLLLGAFPPAAAARGPPKMADKVVPRQVARLGRTVRLQCPVEGDPPPLTM  
WTKDGRTIHSWRSRFRVLPQGLKVKQVEREDAGVYVCKATNGFGSLSVNYTLVVLDISP  
ESLGPDSSSSGGQEDPASQQWARPRFTQPSKMRRRVIA R PVGSSVRLKCVASGHPRPDITWMK  
DDQALTRPEAAEPRKKKWTLSLKNLRPEDSGKYTCRVSNRAGAINATYKVDVIQRTRSKPVL  
TGTHPVNTTVDFGGTTSFQCKVRSDVKPVIQWLKRVEYGAEGRHNSTIDVGGQKFVVLPTGD  
VWSRPDGSYLNKLLITRARQDDAGMYICLGANTMGYSFRSAFLTVLPDPKPPGPPVASSSSA  
TSLPWPVVIGIPAGAVFILGTLLLWLCQAQKKPCTPAPAPPLPGHRPPGTARDRSGDKDLPS  
LAALSAGPGVGLCEEHGSPAAPQHLLGPGPVAGPKLYPKLYTDIHTHTHTSHHTSHVEGKV  
HQHIHYQC

71/330

**FIGURE 71**

CCCAGCTGAGGAGCCCTGCTCAAGACACGGTCACTGGATCTGAGAACTTCCCAGGGGACCGCATTCCAGAGTC  
AGTGACTCTGTGAAGCACCCACATCTACCTCTTGCCACGTTCCACAGGGCTTGGGGGAAAG**ATGGT**GGGGACCA  
AGGCCCTGGGTGTTCTCCTTCTGGTCTGGAAGTCACATCTGTGTTGGGGAGACAGATGCTCACCCAGTCA  
GTAAGAAGAGTCCAGCCTGGGAAGAAGAACCACAGCATCTTTGCCAAGCCTGCCGACACCCTGGAGAGCCCTGG  
TGAGTGGACAACATGGTTCAACATCGACTACCCAGGCGGGAAGGCGACTATGAGCGGCTGGACGCCATTGCT  
TCTACTATGGGGACCGTGTATGTGCCCGTCCCTGCGGCTAGAGGCTCGGACCACTGACTGGACACCTGCGGGC  
AGCACTGGCCAGGTGGTCCATGGTAGTCCCCGTGAGGGTTTCTGGTGCCTCAACAGGGAGCAGCGGCCTGGCCA  
GAACTGCTCTAATTACACCGTACGCTTCTCTGCCACAGGATCCCTGCGCCGAGACACAGAGCGCATCTGGA  
GCCCATGGTCTCCCTGGAGCAAGTGCTCAGCTGCCTGTGGTCAAGTGGGCTCCAGACTCGCACACGCATTTGC  
TTGGCAGAGATGGTGTGCTGTGAGTGAGGCGAGCGAAGAGGGTCAAGCACTGCATGGGCCAGGACTGTACAGC  
CTGTGACCTGACCTGCCAATGGGCGAGTGAATGCTGACTGTGATGCTGCATGTGCCAGGACTTCATGCTTC  
ATGGGGCTGTCTCCCTTCCCGGAGGTGCCCCAGCCTCAGGGGCTGCTATCTACCTCCTGACCAAGACGCCGAAG  
CTGCTGACCCAGACAGACAGTGTATGGGAGATTCCGAATCCCTGGCTTGTGCCCTGATGGCAAAGCATCTTGAA  
GATCACAAAGGTCAAGTTTGGCCCCATTGTACTACAATGCCAAGACTAGCCTGAAGGACACCACTCAAGG  
CAGAGTTTGTGAGGGCAGAGACTCCATAGTGTGATGAACCTGAGACAAAAGCAGGAGAGCTGGGCAGAGC  
GTGTCTGTGCTGTAAAGGCCACAGGGAAGCCAGGCCAGACAAAGTATTTTGGTATCATAATGACACATTGCA  
GGATCCTTCCCTGCTAAGCATGAGAGCAAGCTGGTGCTGAGGAACTGCAGCAGCAGGATAATGGGATGAGTCT  
TTTGCAAGGCCCAGAGTGTGCTGGGGCTGTGAAGTCCAAGGTTGCCAGCTGATTGTACAGCATCTGATGAG  
ACTCCTTGAACCCAGTTCTGTGAGAGTATCTTATCCGGCTGCCCATGATTGCTTTGAGAATGCCACCACTC  
TGCTGACAATGGGGAGCCCATGCGCTTGGCCATGTGTACATGGGGAACAGCCGTGTAAGCATGACTGGCTGCA  
ATGCTGTGCAGAACTGCTGTGGCATCTCCAAGACAGAGGAAAGGGAGATCCAGTGCAGTGGCTACACGCTACCC  
ACCAAGGTGGCCAAAGGATGCAGTGCAGCGGTGTACGGAATCCGAGCATCGGAGCATCGTGCGGGGCGCTGTGCTG  
TGCTGACAATGGGGAGCCCATGCGCTTGGCCATGTGTACATGGGGAACAGCCGTGTAAGCATGACTGGCTGCA  
AGGGCACTTTTACCCTCCATGTCCCCAGGACACTGAGAGGCTGGTGTACATTTGTGGACAGGCTGCAGAAG  
TTTGTCAACACCACCAAGTGTACCTTTCAACAAGAAGGGGAGTGCCGTGTTCCATGAAATCAAGATGCTTCCG  
TCGGAAGAGCCCATCACTTTGGAAGCCATGGAGCAACATCATCCCCCTGGGGGAAGTGGTTGGTGAAGACC  
CCATGGCTGAAGTGGAGATTCCATCCAGGAGTTTCTACAGGCAGAATGGGGAGCCCTACATAGGAAAAGTGAAG  
GCCAGTGTGACCTTCTGGATCCCCGGGAATATTTCCACAGCCACAGCTGCCAGACTGACCTGAACCTCATCAA  
TGACGAAGGAGCACTTTCCCCCTTCGGACGTATGGCATGTTCTCTGTGGACTTCAGAGATGAGGTACCTCAG  
AGCCACTTAATGCTGGCAAAGTGAAGGTCCACCTTGACTCGACCCAGGTCAAGATGCCAGAGCACATATCCACA  
GTGAAACTCTGGTCACTCAATCCAGACACAGGGCTGTGGGAGGAGGAAGGTGATTTCAAATTTGAAAATCAAAG  
GAGGAACAAAAGAGAAGACAGAACCTTCTGGTGGCAACCTGGAGATTCTGTGAGAGGAGTCTTTAACTTGG  
ATGTTCTTGAAGCAGGCGGTGCTTTGTTAAGGTGAGGGCCTACCGGAGTGAGAGGTTCTTGCCCTAGTGAGCAG  
ATCCAGGGGGTGTGATCTCCGTGATTAACCTGGAGCTTGAAGTGGCTTCTTGTCCAACCTTAGGGCCTGGGG  
CCGCTTTGACAGTGTATCACAGGCCCAACCGGGCTGTGTGCCTGCCTTCTGTGATGACCACTGCCCTGATG  
CCTACTCTGCCTATGTCTTGGCAAGCCTGGCTGGGGAGGAACTGCAAGCAGTGGAGTCTTCTCCTAAATTCAAC  
CCAAATGCAATTGGCGTCCCTCAGCCCTATCTCAACAAGCTCAACTACCGTCCGACGGACCATGAGGATCCACG  
GGTTAAAAAGACAGCTTTTCCAGATTAGCATGGCCAAGCCAAGGCCAACTCAGCTGAGGAGAGCAATGGGCCCA  
TCTATGCCCTTTGAGAACCTCCGGGCATGTGAAGAGGCACCACCCAGTGCAGCCCACTTCCGGTTCTACCAGATT  
GAGGGGGATCGATATGACTACAACACAGTCCCCCTCAACGAAGATGACCTATGAGCTGGACTGAAGACTATCT  
GGCATGGTGGCCAAAGCCGATGGAATTGAGGGCTGCTATATCAAGGTGAAGATTGTGGGGCACTGGAAGTGA  
ATGTGCGATCCCGCAACATGGGGGGCACTCATCGGCGGACAGTGGGGAAGCTGTATGGAATCCGAGATGTGAGG  
AGCACTCGGGACAGGGACAGCCCAATGTCTCAGTGCCTGTCTGGAGTTCAAGTGCAGTGGGATGCTCTATGA  
TCAGGACCGTGTGGACCGCACCTGGTGAAGGTCAATCCCCAGGGCAGCTGCCGTGAGCCAGTGTGAACCCCA  
TGCTGCATGAGTACCTGGTCAACCACTTGCCACTTGCACTCAACAACGACACCAGTGAATACCATGCTGGCA  
CCCTTGGACCCACTGGGGCCACAATATGGCATCTACACTGTCACTGACCAGGACCCCTCGCACGGCCAAGGAGAT  
CGCGCTCGGCCGCTGCTTTGATGGCACATCCGATGGCTCCTCCAGAATCATGAAGAGCAATGTGGGAGTAGCCC  
TCACCTTCAACTGTGTAGAGAGGCAAGTAGGCCGCCAGAGTGCCTTCCAGTACCTCAAAGCACCCAGCCAG  
TCCCTTGCTGCAGGCACTGTCCAAGGAAGAGTGCCCTCGAGGAGGACAGCAGCGAGCGAGCAGGGGTGGCCAGCG  
CCAGGGTGGAGTGGTGGCTCTCTGAGATTTCTAGAGTTGCTCAACAGCCCTGATCAAC**TAA**GTTTTGTGGT  
ACTTACCCTCTTCTGCCCTCATTTTCTGTGACAGCCATTGTGAGACTGATGCACAACTGTCACTTGGTTAAT  
TTAAGCACTTCTGTTTTCTGTGAATTTGCTTGTGTTTCTTCTATGCCTTTACTTACTTTGTCCTATGCTACTGA  
TTGGCACGTGGCCCCACAATGGCACAATAAAGCCCCCTTGTGAAACTGTTCTTTAAATGAAACACAAGAAATT  
GGCCACTGGTAAAACTCTGCAGCTTCAACTGACTTCAATTTAATGCCATTAATGCAATATACTTCTCTTCTT  
TTTGCAATGGTTTTGGCCACCTCTGCAATAGTGATAATCTGATGCTGAAGATCAAATAACCAATATAAAGCATAT  
TTCTTGGCCTTGTCTCCACAGGACATAGGCAAGCCTTGATCATAGTTTATACATATAAATGGTGGTGAATAAAG  
AAATAAAACACAATACTTTTACTTGAAATGTAAATAACTTATTTATTTCTTTGCTAAATTTGGAATTTCTAGTGC  
ACATTCAAAGTTAAGCTATTAATATAGGGTGATCATAGTTCTCTACCAAGTCTGGAAAGAACATCTCCTGGT  
ATCCACAATTACACAGGTTGCTAAGTGTATTTGTACATTTTCCCTTTGCTTTGCTTTGCTTAGAAAC  
CCAGTGTAGCCAGGGCAGATGTCAATAAATGCATACTCTGTATTTGAAAAA

72/330

**FIGURE 72**

MVGTKAWVFSFLVLEVTSVLGRQTMLTQSVRRVQPGKKNPSIFAKPADTLESPGEWTTWFNI  
DYPGGKGDYERLDAIRFYYGDRVCARPLRLEARTTDWTPAGSTGQVVHGSPREGFWCLNREQ  
RPGQNC SNYTVRFLCPPGSLRRDTERIWSPWSPWSKCSAACGQTGVQTRTRICLAEMVSLCS  
EASEEGQHCMGQDCTACDLTCPMGQVNADCDACMCQDFMLHGAVSLPGGAPASGAAYLLTK  
TPKLLTQTDSDGRFRI PGLCPDGKSILKITKVKFAPIVLTMPKTSKKAATIKAEFVRAETPY  
MVMNPETKARRAGQSVSLCCKATGKPRPDKYFWYHNDTLLDPSLYKHESKLVLRKLQHQAG  
EYFCKAQSDAGAVKSKVAQLIVTASDET PCNPVPESYLIRLPHDCFQ NATNSFYFDVGRCPV  
KTCAGQQDNGIRCRDAVQNCCGISKTEEREIQCSGYTLPTKVAKESCQRCTETRSIVRGRV  
SAADNGEPMRF GHVYMGN SRVSMTGYKGTFTLHVPQDTERLVLT FVDRLQKFVNTTKVLPFN  
KKGS AVFHEIKMLRRKEPITLEAMETNII PLGEVVGEDPMAELEI PSRSFYRQNGEPYIGKV  
KASVTFLDPRNI STATAAQTDLNF INDEGDTFPLRTYGMFSVDFRDEVTSEPLNAGKVKVHL  
DSTQVKMPEHISTVKLWSLNPDTGLWEEEGDFKFENQRRNKREDRTFLVGNLEIRERRLFNL  
DVPESRRCFVKVRAYR SERFLPSEQIQGVVISVINLEPRTGFLSNPRAWGRFDSVITGPNGA  
CVPAFCDDQSPDAYSAYVLASLAGEELQAVESSPKFNPNAIGVPQPYLNKLNRYRRTDHEDPR  
VKKTAFQISMAKPRPNSAEESNGPIYAFENLRACEEAPPSAAHFRFYQIEGDRYDYNTPFNP  
EDDPM SWTEDYLAWWPKPMEFRACYIKVKIVGPLEVNVR SRNMGGTHRRTVGKLYGIRDVRS  
TRDRDQPNVSAACLEFKCSGMLYDQDRVDRTL VKVIPQGSCRRASVNPMLHEYLVNHLPLAV  
NNDTSEYTMLAPLDPLGHNYGIYTVTDQDPRTAKEIALGRCFDGTS DGSSRIMKSNVGVALT  
FNCVERQVGRQSAFQYLQSTPAQSPAAGTVQGRVPSRRQQRASRGGQRQGGVVASLRFPRVA  
QQPLIN

73/330

**FIGURE 73**

CTGCAAGTTGTTAACGCCTAACACACAAGTATGTTAGGCTTCCACCAAAGTCCTCAATATACCTGAATACGCAC  
AATATCTTAACTCTTCATATTTGGTTTTGGGATCTGCTTTGAGGTCCCATCTTCATTTAAAAAAAATACAGAG  
ACCTACCTACCCGTACGCATACATACATATGTGTATATATATGTAAACTAGACAAAGATCGCAGATCATAAAGC  
AAGCTCTGCTTTAGTTTTCCAAGAAGATTACAAAGAATTTAGAGATGTATTTGTCAAGATCCCTGTCTGATTCATG  
CCCTTTGGGTTACGGTGTCTCAGTGATGCAGCCCTACCCTTTGGTTTTGGGGACATTATGATTTGTGTAAGACT  
CAGATTTACACGGAAGAAGGGAAAGTTTGGGATTACATGGCCTGCCAGCCGGAATCCACGGACATGACAAAATA  
TCTGAAAGTGAAACTCGATCCTCCGGATATTACCTGTGGAGACCCTCCTGAGACGTTCTGTGCAATGGGCAATC  
CCTACATGTGCAATAATGAGTGTGATGCGAGTACCCCTGAGCTGGCACACCCCCCTGAGCTGATGTTTGATTTT  
GAAGGAAGACATCCCTCCACATTTTGGCAGTCTGCCACTTGGAAGGAGTATCCCAAGCCTCTCCAGGTTAACAT  
CACTCTGTCTTGGAGCAAAACCATTGAGCTAACAGACAACATAGTTATTACCTTTGAATCTGGGCGTCCAGACC  
AAATGATCCTGGAGAAGTCTCTCGATTATGGACGAACATGGCAGCCCTATCAGTATTATGCCACAGACTGCTTA  
GATGCTTTTTCACATGGATCCTAAATCCGTGAAGGATTTATCACAGCATACGGTCTTAGAAATCATTTCACACAGA  
AGAGTACTCAACAGGGTATACAACAAATAGCAAAATAATCCACTTTGAAATCAAAGACAGGTTCTCGCGCTTTTGTG  
CTGGACCTCGCCTACGCAATATGGCTTCCCTCTACGGACAGCTGGATACAACCAAGAACTCAGAGATTTCTTT  
ACAGTCACAGACCTGAGGATAAGGCTGTTAAGACCAGCCGTTGGGGAAATATTTGTAGATGAGCTACACTTGGC  
ACGCTACTTTTTACGCGATCTCAGACATAAAGGTGCGAGGAAGGTGCAAGTGTAAATCTCCATGCCACTGTATGTG  
TGTATGACAACAGCAAAATTGACATGCGAATGTGAGCACAACTACAGGTCCAGACTGTGGGAAATGCAAGAAG  
AATTATCAGGGCCGACCTTGGAGTCCAGGCTCCTATCTCCCCATCCCCAAAGGCACTGCAAATACCTGTATCCC  
CAGTATTTCCAGTATTGGTACGAATGTCTGCGACAACGAGCTCCTGCACTGCCAGAACGGAGGGACGTGCCACA  
ACAACGTGCGCTGCCTGTGCCCCGGCCGCATACACGGGCATCCTCTGCGAGAAGCTGCGGTGCGAGGAGGCTGGC  
AGCTGCGGCTCCGACTCTGGCCAGGGCGCGCCCCCGCACGGCACCCAGCGCTGCTGCTGCTGACCACGCTGCT  
GGGAACCGCCAGCCCCCTGGTGTCTTAGGTGTACCTCCAGCCACACCGGACGGGCTGTGCCGTGGGGAAGCA  
GACACAACCCAAACATTTGCTACTAACATAGGAAACACACACATACAGACACCCCCACTCAGACAGTGTACAAA  
CTAAGAAGGCCTAACTGAACTAAGCCATATTTATCACCCGTGGACAGCACATCCGAGTCAAGACTGTTAATTTT  
TGACTCCAGAGGAGTTGGCAGCTGTTGATATTATCACTGCAAATCACATTGCCAGCTGCAGAGCATATTGTGGA  
TTGGAAAGGCTGCGACAGCCCCCAACAGGAAAGACAAAAACAAACAAATCAACCGACCTAAAAACATTGGC  
TACTCTAGCGTGGTGCGCCCTAGTACGACTCCGCCAGTGTGTGGACCAACCAAAATAGCATTCTTTGCTGTCTAG  
GTGCATTGTGGGCATAAGGAAATCTGTTACAAGCTGCCATATTGGCCTGCTTCCGTCCCTGAATCCCTTCCAAC  
CTGTGCTTTAGTGAACGTTGCTCTGTAAACCTCGTTGGTTGAAAGATTTCTTTGTCTGATGTTAGTGATGCACA  
TGTGTAACAGCCCCCTCTAAAAGCGCAAGCCAGTCATACCCCTGTATATCTTAGCAGCACTGAGTCCAGTGCGA  
GCACACACCCACTATACAAGAGTGGCTATAGGAAAAAGAAAGTGTATCTATCCTTTTGTATTCAAATGAAGTT  
ATTTTCTTGAACACTGTAATATGTAGATTTTTTGTATTATTGCCAATTTGTGTTACCAGACAATCTGTTAAT  
GTATCTAATTCGAATCAGCAAAGACTGACATTTTATTTTGTCTCTTTCTGTTCTGTTTGTCTTCACTGTGCAGA  
GATTTCTCTGTAAAGGCAACGAACGTGCTGGCATCAAAGAATATCAGTTTACATATATAACAAGTGAATAAGA  
TTCCACCAAAGGACATTCTAAATGTTTTCTTGTGCTTTAACACTGGAAGATTTAAAGAATAAAAACTCCTGCA  
TAAACGATTTTCAAGGAATTTGTATTGCAATTTCTTAAGATGAAAGGAACAGCCACCAAGCAGTTTCACTCACT  
TTACTGATTTCTGTGTGGACTGAGTACATTCAGCTGACGAATTTAGTTCCAGGAAGATGGATTGATGTTCACT  
AGCTTGACAACTTCTGCAAAATATGAGACTATTTCCACTTGGGAAAAATTACAACAGCAAAAAAAAAAAAAA  
AAAAAA

74/330

**FIGURE 74**

MYLSRSLSIHALWVTVSSVMQPYPLVWGHYDLCKTQIYTEEGKVWDYMACQPESTDMTKYLK  
VKLDPPDITCGDPPETFCAMGNPYMCNNECDASTPELAHPPELMFDFEGRHPSTFWQSATWK  
EYPKPLQVNITLSWSKTIELTDNIVITFESGRPDQMILEKSLDYGRTWQPYQYYATDCLDAF  
HMDPKSVKDLSQHTVLEIICTEEYSTGYTTNSKIIHFEIKDRFALFAGPRLRNMASLYGQLD  
TTKKLRDFFTVDLRLRLLRPAVGEIFVDELHLARYFYAISDIKVRGRCKCNLHATVCVYDN  
SKLTCECEHNTTGPDCGKCKKNYQGRPWSPGSYLPIPKGTANTCIPSISSIGTNVCDNELLH  
CQNGGTCHNNVRCLCPAAYTGILCEKLRCEEAGSCGSDSGQGAPPHGTPALLLLTTLLGTAS  
PLVF

75/330

**FIGURE 75**

CCCACGCGTCCGGGTGACCTGGGCCGAGCCCTCCCGGTCGGCTAAGATTGCTGAGGAGGCGG  
CGGGTAGCTGGCAGGCGCCGACTTCCGAAGGCCGCGTCCGGGCGAGGTGTCCTCATGACTT  
CTCTTGTGGACC**ATG**TCCGTGATCTTTTTTGCCTGCGTGGTACGGGTAAGGGATGGACTGCC  
CCTCTCAGCCTCTACTGATTTTTTACCACACCCAAGATTTTTTGAATGGAGGAGACGGCTCA  
AGAGTTTAGCCTTGC GACTGGCCCAGTATCCAGGTCGAGGTTCTGCAGAAGGTTGTGACTTT  
AGTATACATTTTTTCTTCTTTCGGGGACGTGGCCTGCATGGCTATCTGCTCCTGCCAGTGTCC  
AGCAGCCATGGCCTTCTGCTTCCTGGAGACCCTGTGGTGGGAATTCACAGCTTCCTATGACA  
CTACCTGCATTGGCCTAGCCTCCAGGCCATACGCTTTTCTTGAGTTTGACAGCATCATT CAG  
AAAGTGAAGTGGCATTTTAACTATGTAAGTTCCTCTCAGATGGAGTGCAGCTTGGA AAAAAT  
TCAGGAGGAGCTCAAGTTGCAGCCTCCAGCGGTTCTCACTCTGGAGGACACAGATGTGGCAA  
ATGGGGTGATGAATGGTCACACACCGATGCACTTGGAGCCTGCTCCTAATTTCCGAATGGAA  
CCAGTGACAGCCCTGGGTATCCTCTCCCTCATTCTCAACATCATGTGTGCTGCCCTGAATCT  
CATTTCGAGGAGTTCACCTTGCAGAACATTCTTTACAGGATCCAAGGAGCTGGTTCTGCTGGT  
TGGACCAAACCTCG**TGA**GCCAGCCACCCCTGACCCAAATGAGGAGAGCTCTGATTCTCCCAT  
CCGGGAGCAGTGATGTCAAACCTCTGCTGCTGGGGAAATCTCATCAGCAGGGAGCCTGTGGA  
AAAGGGCATGTCAGTGAAATCTGGGAATGGCTGGATTTCGGAAACATCTGCCCATGTGTATTG  
ATGGCAGAGCTGTTGCCCACAAGCGCCTTTTATTTAGGGTAAAATTAACAAATCCATTCTAT  
TCCTCTGACCCATGCTTAGTACATATGACCTTTAACCCTTACATTTATATGATTCTGGGGTT  
GCTTCAGAAGTGTTATTTTCATGAATCATTCATATGATTTGATCCCCCAGGATTCTATTTTGT  
TTAATGGGCTTTTCTACTAAAAGCATAAAATACTGAGGCTGATTTAGTCAGGGCAAAACCAT  
TTACTTTACATATTCGTTTTCAATACTTGCTGTTTACGTACACAAGCTTCTTACGGTTTTTC  
TTGTAACAATAAATATTTTGAGTAAATAATGGGTACATTTTAACAAACTCAGTAGTACAACC  
TAAACTTGATATAAAAGTGTGTAAAAATGTATAGCCATTTATATCCTATGTATAAATTAAATG  
AGGTGGCTTCAGAAATGGCAGAATAAATCTAAAGTGTTTATTAAAAA AAAAAAAAAAAAAA  
AAAAG



76/330

**FIGURE 76**

MSVIFFACVVRVRDGLPLSASTDFYHTQDFLEWRRRLKSLALRLAQYPGRGSAEGCDFS IHF  
SSFGDVACMAICSCQCPAAMAFCFLETLWWEFTASYDTTCIGLASRPYAFLEFDSIIQKVKW  
HFNYVSSSQMECSLEKIQEELKLQPPAVLTLEDTDVANGVMNGHTPMHLEPAPNFRMEPVTA  
LGILSLILNIMCAALNLIRGVHLAEHSLQDPRSWFCWLDQTS

77/330

**FIGURE 77**

TGCTTCCTGGAGACCCCTGTGGTGGGAATTCACAGCTTCNTATGACACTACCTGCATTGGCNT  
AGCCTCCAGGCCATACGCTTTTCTTGAGTTTGACAGCATCATTGAGAAAGTGAAGTGGCATT  
TTAACTATGTAAGTTCCTNTCAGATGGAGTGCAGCTTGAAAAAATTCAGGAGGAGCTCAAG  
TTGCAGCCTCCAGCGGTTCTCANTATGGAGGACACAGATGTGGCAAATGGGGT

78/330

**FIGURE 78**

CTCAGCGGGCGCTTCCTCGTAGCGAGCCTAGTGGCGGGTGTTCGATTGAAACGTGAGCGCGA  
CCCGACCTTAAAGAGTGGGGAGCAAAGGGAGGACAGAGCCCTTTAAAACGAGGCGGGTGGTG  
CCTGCCCCCTTTAAGGGCGGGGCGTCCGGACGACTGTATCTGAGCCCCAGACTGCCCCGAGTT  
TCTGTGCGCAGGCTGCGAGGAAAGGCCCTAGGCTGGGTCTGGGTGCTTGGCGGCGGCGGCTT  
CCTCCCCGCTCGTCCCTCCCCGGGCCCAGAGGCACCTCGGCTTCAGTCATGCTGAGCAGAGTA  
TGGGAAGCACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGC  
GAGTGTATTATATCAACACTTCTGTTTGCAACACTGTACATCCTCTGCCACATCTTCCTGAC  
CCGCTTCAAGAAGCCTGCTGAGTTCACCACAGTGGATGATGAAGATGCCACCGTCAACAAGA  
TTGCGCTCGAGCTGTGCACCTTTACCCTGGCAATTGCCCTGGGTGCTGTCTGCTCCTGCCC  
TTCTCCATCATCAGCAATGAGGTGCTGCTCTCCCTGCCTCGGAACACTACTACATCCAGTGGCT  
CAACGGCTCCCTCATCCATGGCCTCTGGAACCTTGTTTTCTCTTCCCCAACCTGTCCCTCA  
TCTTCCTCATGCCCTTTGCATATTTCTTCACTGAGTCTGAGGGCTTTGCTGGCTCCAGAAAG  
GGTGTCTGCTGGGCCGGGTCTATGAGACAGTGGTGATGTTGATGCTCCTCACTCTGCTGGTGCT  
AGGTATGGTGTGGGTGGCATCAGCCATTGTGGACAAGAACAAGGCCAACAGAGAGTCACTCT  
ATGACTTTTGGGAGTACTATCTCCCTACCTCTACTCATGCATCTCCTTCCTTGGGGTTCTG  
CTGCTCCTGGTGTGTACTCCACTGGGTCTCGCCCGCATGTTCTCCGTCACTGGGAAGCTGCT  
AGTCAAGCCCCGGCTGCTGGAAGACCTGGAGGAGCAGCTGTACTGCTCAGCCTTTGAGGAGG  
CAGCCCTGACCCGCAGGATCTGTAATCCTACTTCCTGCTGGCTGCCTTTAGACATGGAGCTG  
CTACACAGACAGGTCCTGGCTCTGCAGACACAGAGGGTCCTGCTGGAGAAGAGGCGGAAGGC  
TTCAGCCTGGCAACGGAACCTGGGCTACCCCCTGGCTATGCTGTGCTTGCTGGTGCTGACGG  
GCCTGTCTGTGCTCATTGTGGCCATCCACATCCTGGAGCTGCTCATCGATGAGGCTGCCATG  
CCCCGAGGCATGCAGGGTACCTCCTTAGGCCAGGTCTCCTTCTCCAAGCTGGGCTCCTTTGG  
TGCCGTCATTAGGTTGTACTCATCTTTTACCTAATGGTGTCTCAGTTGTGGGCTTCTATA  
GCTCTCCACTCTTCCGGAGCCTGCGGCCCAGATGGCACGACACTGCCATGACGCAGATAATT  
GGGAACTGTGTCTGTCTCCTGGTCCTAAGCTCAGCACTTCCTGTCTTCTCTCGAACCCCTGGG  
GCTCACTCGCTTTGACCTGCTGGGTGACTTTGGACGCTTCAACTGGCTGGGCAATTTCTACA  
TTGTGTTCTCTACAACGCAGCCTTTGCAGGCCTCACCACACTCTGTCTGGTGAAGACCTTC  
ACTGCAGCTGTGCGGGCAGAGCTGATCCGGGCCTTTGGGCTGGACAGACTGCCGCTGCCCGT  
CTCCGGTTTCCCCCAGGCATCTAGGAAGACCCAGCACCAGTGACCTCCAGCTGGGGGTGGGA  
AGGAAAAAACTGGACACTGCCATCTGCTGCCTAGGCCTGGAGGGAAGCCCAAGGCTACTTGG  
ACCTCAGGACCTGGAATCTGAGAGGGTGGGTGGCAGAGGGGAGCAGAGCCATCTGCACTATT  
GCATAATCTGAGCCAGAGTTTGGGACCAGGACCTCCTGCTTTTCCATACTTAACTGTGGCCT  
CAGCATGGGGTAGGGCTGGGTGACTGGGTCTAGCCCCTGATCCCAAATCTGTTTACACATCA  
ATCTGCCTCACTGCTGTTCTGGGCCATCCCCATAGCCATGTTTACATGATTTGATGTGCAAT  
AGGGTGGGGTAGGGGCAGGGAAAGGACTGGGCCAGGGCAGGCTCGGGAGATAGATTGTCTCC  
CTTGCTCTGGCCCAGCAGAGCCTAAGCACTGTGCTATCCTGGAGGGGCTTTGGACCACCTG  
AAAGACCAAGGGGATAGGGAGGAGGAGGCTTCAGCCATCAGCAATAAAGTTGATCCCAGGGA  
AAAAAA

79/330

**FIGURE 79**

MEAPDYEVLSVREQLFHERIRECIISTLLFATLYILCHIFLTRFKKPAEFTTVDDDEDATV NK  
IALELCTFTLAIALGAVLLLPFSIISNEVLLSLPRNYIIQWLNGSLIHGLWNLVFLFPNLSL  
IFLMPFAYFFTESEGFAGSRKGV LGRVYETVVMLMLLTLLVLGMVWVASAIVDKNKANRESL  
YDFWEYYLPYLYSCISFLGVLLLLVCTPLGLARMFSVTGKLLVKPRILLEDLEEQLYCSAFEE  
AALTRRICNPTSCWLPLDMELLHRQVLALQTQRV LLEKRRKASAWQRNLGYPLAMLCLLVLT  
GLSVLIVAIHILELLIDEAAMP RGMQGTSLGQVSFSKLG SFGAVIQVVLIFYLMVSSVVG FY  
SSPLFRSLRPRWHD TAMTQIIIGNCVCLLV LSSALPVFSRTLGLTRFDLLGDFGRFNWLG NFY  
IVFLYNAAFAGLTTLCLVKTF TA AVRAELIRAFGLDRLPLPVSGFPQASRKTQH Q

80/330

**FIGURE 80**

GGCTGCCGAGGGAAGGCCCTTGGGTGGTCTTGGTTGCTTGGCGGCGGCGGNTTCNTCCCC  
GCTCGTCCTCCCCGGGCCAGAGGCACCTCGGCTTCAGTCATGCTGAGCAGAGTATGGAAGC  
ACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGCGAGTGTA  
TTATATCAACACTTCTGTTTGCAACACTGTACATCCTCTGCCACATCTTCCTGACCCGCTTC  
AAGAAGCCTGCTGAGTTCACCACAGTGGATGATGAAGATGCCACCG

81/330

**FIGURE 81**

GACCGACCTTAAAGAGTGGGAGCAAAGGGAGGACAGAGCCTTTTAAAACGAGGCGGTGGTGC  
CTGCCCTTTAAGGGCGGGGCGTCCGGACGACTGTATCTGAGCCCCAGACTGCCCCGAGTTTC  
TGTCGCAGGCTGCGAGGAAAGGCCCCCTAGGCTGGGTCTGGTGCTTGCGGGCGGCGGCTTCCT  
CCCCGTTGTCNTCCCCGGGCCCCAGAGGCACCTCGGCTTCAGTCATGCTGAGCAGAGTATGGA  
AGCACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGCGAGT  
GTATTATATCAACACTTCTGTTTGCAACACTGTACATCNTCTGCCACATCTTCCTGACCCGC  
TTCAAGAAGCCTGCTGAGTTCACCACAGTGATGATGAAGATGCCACCGTCAACAAGATTGC  
GCTCGAGCTGTGCACCTTTACCCTGGCAATTGCCCTGGGTGCTGTCCTGCTCCTGCCCTTCT  
CCATCATCAGCAATGAGGTGCTGCACTCCC

82/330

**FIGURE 82**

GATGTGCTCCTTGGAGCTGGTGTGCAGTGTCTGACTGTAAGATCAAGTCCAAACCTGTTTT  
GGAATTGAGGAACTTCTCTTTTGATCTCAGCCCTTGGTGGTCCAGGTCTTC**ATG**CTGCTGT  
GGTGATATTACTGGTCCTGGCTCCTGTCAGTGGACAGTTTGCAAGGACACCCAGGCCCAT  
ATTTTCCTCCAGCCTCCATGGACCACAGTCTTCCAAGGAGAGAGAGTGACCCTCACTTGCAA  
GGGATTTTCGCTTCTACTCACCACAGAAAACAAAATGGTACCATCGGTACCTTGGGAAAGAAA  
TACTAAGAGAAACCCCAGACAATATCCTTGAGGTTTCAAGGAATCTGGAGAGTACAGATGCCAG  
GCCCAGGGCTCCCCTCTCAGTAGCCCTGTGCACTTGGATTTTTCTTCAGAGATGGGATTTCC  
TCATGCTGCCCAGGCTAATGTTGAACTCCTGGGCTCAAGTGATCTGCTCACCT**TAG**GCCTCTC  
AAAGCGCTGGGATTACAGCTTCGCTGATCCTGCAAGCTCCACTTTCTGTGTTTGAAGGAGAC  
TCTGTGGTTCTGAGGTGCCGGGCAAAGGCGGAAGTAACACTGAATAATACTATTTACAAGAA  
TGATAATGTCCTGGCATTCTTAATAAAAGAACTGACTTCCAAAAAAAAAAAAAAAAAAAAA  
AAA

83/330

**FIGURE 83**

MLLWVILLVLAPVSGQFARTPRPIIFLQPPWTTVFQGERVTLTCKGFRFYSPQKTKWYHRYL  
GKEILRETPDNILEVQESGEYRCQAQGSPLSSPVHLD FSSEMGFPHAAQANVELLGSSDLLT



84/330

**FIGURE 84**

CAGAAGAGGGGGCTAGCTAGCTGTCTCTGCGGACCAGGGAGACCCCCGCGCCCCCCCCGGTGT  
GAGGCGGCCTCACAGGGCCGGGTGGGCTGGCGAGCCGACGCGGCGGCGGAGGAGGCTGTGAG  
GAGTGTGTGGAACAGGACCCGGGACAGAGGAACC**ATG**GCTCCGCAGAACCTGAGCACCTTTT  
GCCTGTTGCTGCTATACCTCATCGGGGCGGTGATTGCCGGACGAGATTTCTATAAGATCTTG  
GGGGTGCCTCGAAGTGCCTCTATAAAGGATATTAAAAAGGCCTATAGGAACTAGCCCTGCA  
GCTTCATCCCGACCGGAACCCTGATGATCCACAAGCCCAGGAGAAATTCCAGGATCTGGGTG  
CTGCTTATGAGGTTCTGTGATAGTGAGAAACGGAAACAGTACGATACTTATGGTGAAGAA  
GGATTAAAAGATGGTCATCAGAGCTCCCATGGAGACATTTTTTTCACACTTCTTTGGGGATTT  
TGGTTTCATGTTTGGAGGAACCCCTCGTCAGCAAGACAGAAATATTCCAAGAGGAAGTGATA  
TTATTGTAGATCTAGAAGTCACTTTGGAAGAAGTATATGCAGGAAATTTTGTGGAAGTAGTT  
AGAAACAAACCTGTGGCAAGGCAGGCTCCTGGCAAACGGAAGTGCAATTGTCGGCAAGAGAT  
GCGGACCACCCAGCTGGGCCCTGGGCGCTTCCAAATGACCCAGGAGGTGGTCTGCGACGAAT  
GCCCTAATGTCAAACCTAGTGAATGAAGAACGAACGCTGGAAGTAGAAATAGAGCCTGGGGTG  
AGAGACGGCATGGAGTACCCCTTTATTGGAGAAGGTGAGCCTCACGTGGATGGGGAGCCTGG  
AGATTTACGTTCCGAATCAAAGTTGTCAAGCACCCAATATTTGAAAGGAGAGGAGATGATT  
TGTACACAAATGTGACAATCTCATTAGTTGAGTCACTGGTTGGCTTTGAGATGGATATTACT  
CACTTGGATGGTCACAAGGTACATATTTCCCGGGATAAGATCACCAGGCCAGGAGCGAAGCT  
ATGGAAGAAAGGGGAAGGGCTCCCCAACTTTGACAACAACAATATCAAGGGCTCTTTGATAA  
TCACTTTTGATGTGGATTTTCCAAAAGAACAGTTAACAGAGGAAGCGAGAGAAGGTATCAAA  
CAGCTACTGAAACAAGGGTCAGTGCAGAAGGTATACAATGGACTGCAAGGATAT**TG**AGAGTG  
AATAAAATTGGACTTTGTTTAAAATAAGTGAATAAGCGATATTTATTATCTGCAAGGTTTTT  
TTGTGTGTGTTTTTGTTTTTATTTTCAATATGCAAGTTAGGCTTAATTTTTTTATCTAATGA  
TCATCATGAAATGAATAAGAGGGCTTAAGAATTTGTCCATTTGCATTGCGAAAAGAATGACC  
AGCAAAAGGTTTACTAATACCTCTCCCTTTGGGGATTTAATGTCTGGTGCTGCCGCCTGAGT  
TTCAAGAATTAAAGCTGCAAGAGGACTCCAGGAGCAAAAGAAACACAATATAGAGGGTTGGA  
GTTGTTAGCAATTTCAATTCAAAATGCCAACTGGAGAAGTCTGTTTTTAAATACATTTTGTG  
TTATTTTTTA

85/330

**FIGURE 85**

MAPQNLSTFCLLLLYLIGAVIAGRDFYKILGVPRSASIKDIKKAYRKLALQLHPDRNPDDPQ  
AQEKFQDLGAAYEVLSDSEKRRKQYDTYGEGLKDGHQSSHGDI FSHFFGDFGFMFGGT PRQQ  
DRNIPRGSDIIVDLEVTLEEYAGNFVEVVRNKPVARQAPGKRKCNCRQEMRTTQLGPGRFQ  
MTQEVVCDECPNVKLVNEERTLEVEIEPGVRDGM EYPFFIGEGEPHVDGEPGDLRFRIKVVKH  
PIFERRGDDLYTNVTISLVESLVGFEMDITHLDGHKVHISRDKITRPGAKLWKKGEGLPNFD  
NNNIKGSLLIITFDVDFPKEQLTEEAREGIKQLLKQGSVQKVYNGLQGY

**Important features:****Signal peptide:**

amino acids 1-22

**Cell attachment sequence.**

amino acids 254-257

**Nt-dnaJ domain signature.**

amino acids 67-87

**Homologous region to Nt-dnaJ domain proteins.**

amino acids 26-58

**N-glycosylation site.**

amino acids 5-9, 261-265

**Tyrosine kinase phosphorylation site.**

amino acids 253-260

**N-myristoylation site.**

amino acids 18-24, 31-37, 93-99, 215-221

**Amidation site.**

amino acids 164-168

86/330

**FIGURE 86**

TGGGACCAGGGAACCCCGGGCCCCCGGTGGAGNGCCTAACAGGCCGGTGGNTGCGACCGAA  
GCGGCGGGCGGAGGAGGTTTTGAGGATTTTTGGAACAGGACCCGGACAGAGGAACCATGGTT  
CCGCAGAACNTGAGCACNTTTTGCCTGTTGNTGNTATACTTCATCGGGGCGGTGATTGCCGG  
ACGAGATTTNTATAAGATTTTGGGGTGCCTNGAAGTGCCTTNTATAAAGGATATTAAAAAGG  
CCTATAGGAAACTAGCCCTGCAGNTTATCCCGACCGGAACCCTGATGATCCACAAGCCCAG  
GAGAAATTCCAGGATTTGGGTGCTGCTTATGAGGTTNTGTCAGATAGTGAGAAACGGAAACA  
GTACGATAATTATGGTGAAGAAGGATTAAAAGATGGTNATCAGAGCTCCCATGGAGACATTT  
TTTCACACTTNTTTGGGGATTTTGGTTTCATGTTTGGAGGAACCCCTNGTCAGCAAGACAGA  
AATATTCCAAGAG

87/330

**FIGURE 87**

GGCACGAGGCGGCGGGGCAGTCGCGGGATGCGCCCGGGAGCCACAGCCTGAGGCCCTCAGGT  
CTCTGCAGGTGTCGTGGAGGAACCTAGCACCTGCCATCCTCTTCCCCAATTTGCCACTTCCA  
GCAGCTTTAGCCCATGAGGAGGATGTGACCGGGACTGAGTCAGGAGCCCTCTGGAAGC**ATGG**  
AGACTGTGGTGATTGTTGCCATAGGTGTGCTGGCCACCATCTTTCTGGCTTCGTTTGCAGCC  
TTGGTGCTGGTTTGCAGGCAGCGCTACTGCCGGCCGCGAGACCTGCTGCAGCGCTATGATTC  
TAAGCCCATTGTGGACCTCATTGGTGCCATGGAGACCCAGTCTGAGCCCTCTGAGTTAGAAC  
TGGACGATGTCGTTATCACCAACCCCCACATTGAGGCCATTCTGGAGAATGAAGACTGGATC  
GAAGATGCCTCGGGTCTCATGTCCCACTGCATTGCCATCTTGAAGATTTGTCACACTCTGAC  
AGAGAAGCTTGTTGCCATGACAATGGGCTCTGGGGCCAAGATGAAGACTTCAGCCAGTGTCA  
GCGACATCATTGTGGTGGCCAAGCGGATCAGCCCCAGGGTGGATGATGTTGTGAAGTCGATG  
TACCTCCGTTGGACCCCCAACTCCTGGACGCACGGACGACTGCCCTGCTCCTGTCTGTCAG  
TCACCTGGTGCTGGTGACAAGGAATGCCTGCCATCTGACGGGAGGCCTGGACTGGATTGACC  
AGTCTCTGTCGGCTGCTGAGGAGCATTGGAAGTCCTTCGAGAAGCAGCCCTAGCTTCTGAG  
CCAGATAAAGGCCTCCCAGGCCCTGAAGGCTTCCTGCAGGAGCAGTCTGCAATTT**TAGT**GCCT  
ACAGGCCAGCAGCTAGCCATGAAGGCCCTGCCGCCATCCCTGGATGGCTCAGCTTAGCCTT  
CTACTTTTTCTATAGAGTTAGTTGTTCTCCACGGCTGGAGAGTTCAGCTGTGTGTGCATAG  
TAAAGCAGGAGATCCCCGTCAGTTTATGCCTCTTTTGCAGTTGCAAACGTGGCTGGTGAGT  
GGCAGTCTAATACTACAGTTAGGGGAGATGCCATTCACTCTCTGCAAGAGGAGTATTGAAAA  
CTGGTGGACTGTCAGCTTTATTTAGCTCACCTAGTGTTTTCAAGAAAATTGAGCCACCGTCT  
AAGAAATCAAGAGGTTTCACATTAAAATTAGAATTTCTGGCCTCTCTCGATCGGTCAGAATG  
TGTGGCAATTCTGATCTGCATTTTCAGAAGAGGACAATCAATTGAACTAAGTAGGGGTTTC  
TTCTTTTGGCAAGACTTGTA CTCTCACCTGGCCTGTTTCATTTATTTGTATTATCTGCCT  
GGTCCCTGAGGCGTCTGGGTCTCTCCTCTCCCTTG CAGGTTTGGGTTTGAAGCTGAGGAACT  
ACAAAGTTGATGATTTCTTTTTTATCTTTATGCCTGCAATTTTACCTAGCTACCACTAGGTG  
GATAGTAAATTTATACTTATGTTTCCCTCAAAAAAAAAAAAAAA

88/330

**FIGURE 88**

METVVIVAIGVLATIFLASFAALVLVCRQRYCRPRDLLQRYDSKPIVDLIGAMETQSEPSEL  
ELDDVVITNPHIEAILENEDWIEDASGLMSHCIAILKICHTLTEKLVAMTMGSGAKMKTSA  
VSDIIVVAKRISPRVDDVVKSMYPPLDPKLLDARTTALLSVSHLVLVTRNACHLTGGLDWI  
DQSLSAEEHLEVLREAALASEPDKGLPGPEGFLQEQSAI

89/330

**FIGURE 89**

GCTTCATTTCTCCCGACTCAGCTTCCCACCCTGGGCTTTCCGAGGTGCTTTCGCCGCTGTCC  
CCACCACTGCAGCC**ATG**ATCTCCTTAACGGACACGCAGAAAATTGGAATGGGATTAACAGGA  
TTTGGAGTGTTTTTCTGTTCTTTGGAATGATTCTCTTTTTTGACAAAGCACTACTGGCTAT  
TGGAAATGTTTTATTTGTAGCCGGCTTGGCTTTTGTAATTGGTTTAGAAAGAACATTCAGAT  
TCTTCTTCCAAAAACATAAAATGAAAGCTACAGGTTTTTTTTCTGGGTGGTGTATTTGTAGTC  
CTTATTGGTTGGCCTTTGATAGGCATGATCTTCGAAATTTATGGATTTTTTCTCTTGTTTCAG  
GGGCTTCTTTCCTGTCGTTGTTGGCTTTATTAGAAGAGTGCCAGTCCTTGATCCCTCCTAAAT  
TTACCTGGAATTAGATCATTTGTAGATAAAGTTGGAGAAAGCAACAATATGGTAT**TAA**CAACA  
AGTGAATTTGAAGACTCATTTAAAATATTGTGTTATTTATAAAGTCATTTGAAGAATATTCA  
GCACAAAATTAAATTACATGAAATAGCTTGTAATGTTCTTTACAGGAGTTTAAAACGTATAG  
CCTACAAAGTACCAGCAGCAAATTAGCAAAGAAGCAGTGAAAACAGGCTTCTACTCAAGTGA  
ACTAAGAAGAAGTCAGCAAGCAAAGTCTGAGAGAGGTGAAATCCATGTTAATGATGCTTAAGAA  
ACTCTTGAAGGCTATTTGTGTTGTTTTTCCACAATGTGCGAAACTCAGCCATCCTTAGAGAA  
CTGTGGTGCCTGTTTCTTTTCTTTTTATTTTGAAGGCTCAGGAGCATCCATAGGCATTTGCT  
TTTTAGAAGTGTCCACTGCAATGGCAAAAATATTTCCAGTTGCACTGTATCTCTGGAAGTGA  
TGCATGAATTCGATTGGATTGTGTCATTTTAAAGTATTAAAACCAAGGAAACCCCAATTTTG  
ATGTATGGATTACTTTTTTTTGNGCNCAGGGCC

90/330

**FIGURE 90**

MISLTDTQKIGMGLTGFGVFFLFFGMILFFDKALLAIGNVLFVAGLAFVIGLERTFRFFFQK  
HKMKATGFFLGGVFVVLIGWPLIGMIFEIYGFFLLFRGFFPVVVGFI RRVPVLGSLLNLPGI  
RSFVDKVGESNNMV

**Important features:****Transmembrane domains:**

amino acids 12-30 (typeII), 33-52, 69-89 and 93-109

**N-myristoylation sites.**

amino acids 11-16, 51-56 and 116-121

**Aminoacyl-transfer RNA synthetases class-II protein.**

amino acids 49-59

91/330

**FIGURE 91**

GAAGACGTGGCGGCTCTCGCCTGGGCTGTTTCCCGGCTTCATTTCTCCCGACTCAGCTTCCC  
ACCNTGGGCTTTCCGAGGTGCTTTCGCCGCTGTCCCCACCACTGCAGCCATGATCTCCTTAA  
CGGACACGCAGAAAATTGGAATGGGATTAACCGGATTTGGAGTGTTTTTCCTGTTCTTTGGA  
ATGATTCTCTTTTTTGACAAAGCACTACTGGCTATTGGAAATGTTTTATTTGTAGCCGGCTT  
GGCTTTTGTAATTGGTTTAGAAAGAACATTCAGATTCTTCTTCCAAAACATAAAATGAAAG  
CTACAGGTTTTTTTCTGGGTGGTGTATTTGTAGTCCTTATTGGTTGGCCTTTGATAGGCATG  
ATCTTCGAAATTTATGGATTTTTTCTCTTGTTT



92/330

**FIGURE 92**

GGCACGAGGCTGAACCCAGCCGGCTCCATCTCAGCTTCTGGTTTCTAAGTCCATGTGCCAAA  
GGCTGCCAGGAAGGAGACGCCTTCCTGAGTCCTGGATCTTTCTTCCTTCTGGAAATCTTTGA  
CTGTGGGTAGTTATTTATTTCTGAATAAGAGCGTCCACGCATCATGACCTCGCGGGACTGC  
TGAAGTCTCAGTTCCTGTGCCACCTGGTCTTCTGCTACGTCTTTATTGCCTCAGGGCTAATC  
ATCAACACCATTTCAGCTCTTCACTCTCCTCCTCTGGCCCATTAACAAGCAGCTCTTCCGGAA  
GATCAACTGCAGACTGTCCTATTGCATCTCAAGCCAGCTGGTGATGCTGCTGGAGTGGTGGT  
CGGGCACGGAATGCACCATCTTCACGGACCCGCGCGCCTACCTCAAGTATGGGAAGGAAAAT  
GCCATCGTGGTTCTCAACCACAAGTTTGAAATTGACTTTCTGTGTGGCTGGAGCCTGTCCGA  
ACGCTTTGGGCTGTTAGGGGGCTCCAAGGTCCTGGCCAAGAAAGAGCTGGCCTATGTCCCAA  
TTATCGGCTGGATGTGGTACTTCACCGAGATGGTCTTCTGTTTCGCGCAAGTGGGAGCAGGAT  
CGCAAGACGGTTGCCACCAGTTTGCAGCACCTCCGGGACTACCCCGAGAAGTATTTTTTTCCT  
GATTCACTGTGAGGGCACACGGTTCACGGAGAAGAAGCATGAGATCAGCATGCAGGTGGCCC  
GGGCCAAGGGGCTGCCTCGCCTCAAGCATCACCTGTTGCCACGAACCAAGGGCTTCGCCATC  
ACCGTGAGGAGCTTGAGAAATGTAGTTTCAGCTGTATATGACTGTACACTCAATTTTCAGAAA  
TAATGAAAATCCAACACTGCTGGGAGTCCTAAACGGAAAGAAATACCATGCAGATTTGTATG  
TTAGGAGGATCCCCTGGAAGACATCCCTGAAGACGATGACGAGTGCTCGGCCTGGCTGCAC  
AAGCTCTACCAGGAGAAGGATGCCTTTCAGGAGGAGTACTACAGGACGGGCACCTTCCGAGA  
GACGCCCATGGTGCCCCCCCCGGCGGCCCTGGACCCTCGTGAACTGGCTGTTTTGGGCCTCGC  
TGGTGCTCTACCCTTTCTTCCAGTTCCTGGTCAGCATGATCAGGAGCGGGTCTTCCCTGACG  
CTGGCCAGCTTCATCCTCGTCTTCTTTGTGGCCTCCGTGGGAGTTCGATGGATGATTGGTGT  
GACGGAAATTGACAAGGGCTCTGCCTACGGCAACTCTGACAGCAAGCAGAACTGAATGACT  
GACTCAGGGAGGTGTCACCATCCGAAGGGAACCTTGGGGAACCTGGTGGCCTCTGCATATCCT  
CCTTAGTGGGACACGGTGACAAAGGCTGGGTGAGCCCCTGCTGGGCACGGCGGAAGTCACGA  
CCTCTCCAGCCAGGGAGTCTGGTCTCAAGGCCGGATGGGGAGGAAGATGTTTTGTAATCTTT  
TTTTCCCCATGTGCTTTAGTGGGCTTTGGTTTTCTTTTTGTGCGAGTGTGTGTGAGAATGGC  
TGTGTGGTGAGTGTGAACTTTGTTCTGTGATCATAGAAAGGTATTTTAGGCTGCAGGGGAG  
GGCAGGGCTGGGGACCGAAGGGGACAAGTTCCCCTTTCATCCTTTGGTGCTGAGTTTTCTGT  
AACCCTTGGTTGCCAGAGATAAAGTGAAAAGTGCTTTAGGTGAGATGACTAAATTATGCCTC  
CAAGAAAAAAAATTAAAGTGCTTTTCTGGGTCAAAAAAAAAAAAA

93/330

**FIGURE 93**

MDLAGLLKSQFLCHLVFCYVFIA SGLIINTIQLFTLLLWPINKQLFRKINCRLSYCISSQLV  
MLLEWWSGTECTIFTDPRAYLKYGKENAIVVLNHNKFEIDFLCGWSLSERFGLLGSKVLAKK  
ELAYVPIIGWMWYFTEMVFCSRKWEQDRKTVATSLQHLDYPEKYFFLIHCEGTRFTEKKHE  
ISMQVARAKGLPRLKHHLLPRTKGFAITVRSLRNVVSAVYDCTLNFRNNENPTLLGVLNGKK  
YHADLYVRRIPLEDIPEDDDECSAWLHKLYQEKDAFQEEYYRTGTFFETPMVPPRRPWTLVN  
WLFWASLVLYPFFQFLVSMIRSGSSLTLASFILVFFVASVGVRWMIGVTEIDKGSAYGNSDS  
KQKLND

94/330

**FIGURE 94**

CTGAGGCGGCGGTAGC**ATG**GAGGGGGAGAGTACGTCGGCGGTGCTCTCGGGCTTTGTGCTCG  
GCGCACTCGCTTTCCAGCACCTCAACACGGACTCGGACACGGAAGGTTTTCTTCTTGGGGAA  
GTAAAAGGTGAAGCCAAGAACAGCATTACTGATTCCCAAATGGATGATGTTGAAGTTGTTTA  
TACAATTGACATTCAGAAATATATTCCATGCTATCAGCTTTTGTAGCTTTTATAATTCTTCAG  
GCGAAGTAAATGAGCAAGCACTGAAGAAAATATTATCAAATGTCAAAAAGAATGTGGTAGGT  
TGGTACAAATTCCGTCGTCATTCAGATCAGATCATGACGTTTAGAGAGAGGCTGCTTCACAA  
AACTTGCAGGAGCATTTTTCAAACCAAGACCTTGTTTTTCTGCTATTAACACCAAGTATAA  
TAACAGAAAGCTGCTCTACTCATCGACTGGAACATTCCTTATATAAACCTCAAAAAGGACTT  
TTTCACAGGGTACCTTTAGTGTTGTTGCCAATCTGGGCATGTCTGAACAACTGGGTTATAAAAC  
TGTATCAGGTTCCCTGTATGTCCACTGGTTTTAGCCGAGCAGTACAAACACACAGCTCTAAAT  
TTTTTGAAGAAGATGGATCCTTAAAGGAGGTACATAAGATAAATGAAATGTATGCTTCATTA  
CAAGAGGAATTAAAGAGTATATGCAAAAAAGTGGAAGACAGTGAACAAGCAGTAGATAAACT  
AGTAAAGGATGTAAACAGATTAAAACGAGAAATTGAGAAAAGGAGAGGAGCACAGATTCAGG  
CAGCAAGAGAGAAGAACATCCAAAAGACCCTCAGGAGAACATTTTTCTTTGTCAGGCATTA  
CGGACCTTTTTTCCAAATCTGAATTTCTTCATTCATGTGTTATGTCTTTAAAAAATAGACA  
TGTTTCTAAAAGTAGCTGTAACCTACAACCACCATCTCGATGTAGTAGACAATCTGACCTTAA  
TGGTAGAACACACTGACATTCCTGAAGCTAGTCCAGCTAGTACACCACAAATCATTAAAGCAT  
AAAGCCTTAGACTTAGATGACAGATGGCAATTCAGAGATCTCGGTTGTTAGATACACAAGA  
CAAACGATCTAAAGCAAATACTGGTAGTAGTAACCAAGATAAAGCATCCAAAATGAGCAGCC  
CAGAAACAGATGAAGAAATTGAAAAGATGAAGGGTTTTGGTGAATATTCACGGTCTCCTACA  
TTTT**TGA**TCCTTTTAACTTACAAGGAGATTTTTTTTATTTGGCTGATGGGTAAAGCCAAACAT  
TTCTATTGTTTTTACTATGTTGAGCTACTTGCAGTAAGTTCATTTGTTTTTACTATGTTTAC  
CTGTTTGCAGTAATACACAGATAACTCTTAGTGCATTTACTTCACAAAGTACTTTTTCAAAC  
ATCAGATGCTTTTTATTTCCAAACCTTTTTTTTACCTTTCACTAAGTTGTTGAGGGGAAGGCT  
TACACAGACACATTCCTTTAGAATTGGAAAAGTGAGACCAGGCACAGTGGCTCACACCTGTAA  
TCCCAGCACTTAGGGAAGACAAGTCAGGAGGATTGATTGAAGCTAGGAGTTAGAGACCAGCC  
TGGGCAACGTATTGAGACCATGTCTATTAATAAATAAATGGAAGCAAGAATAGCCTTAT  
TTTCAAAATATGGAAAGAAATTTATATGAAAATTTATCTGAGTCATTAAAATTCCTCCTTAAG  
TGATACTTTTTTGAAGTACATTATGGCTAGAGTTGCCAGATAAATGCTGGATATCATGCA  
ATAAATTTGCAAAACATCATCTAAAATTTAAAAAAAAAAAAAAAAAAAAAAAAA

95/330

**FIGURE 95**

MEGESTSAVLSGFVLGALAFQHLNTDSDTEGFLLGEVKGEAKNSITDSQMDDVEVVYTIDIQ  
KYIPCYQLFSFYNSSGEVNEQALKKILSNVKNVVGWYKFRRHSDQIMTFRERLLHKNLQEH  
FSNQDLVFLLLTPSIITESCSTHRLEHSLYKPQKGLFHRVPLVVANLGMSEQLGYKTVSGSC  
MSTGFSRAVQTHSSKFFEEEDGSLKEVHKINEMYASLQEELKSICKKVEDSEQAVDKLVKDVN  
RLKREIEKRRGAQIQAAAREKNIQKDPQENIFLCQALRTFFPNSEFLHSCVMSLKNRHVSKSS  
CNYNHHLDVVDNLTLMVEHTDIPEASPASTPQIIKHKALDLDLDRWQFKRSRLDLDQDKRSKA  
NTGSSNQDKASKMSSPETDEEIEKMKGFGEYSRSPTF

96/330

**FIGURE 96**

GGCACAGCCGCGCGGGCGGAGGGCAGAGTCAGCCGAGCCGAGTCCAGCCGGACGAGCGGACCAGCGCAGGGCAGC  
CCAAGCAGCGCGCAGCGAACGCCCCGCCGCCGCCACACCCTCTGCGGTCCCCGCGGCGCCTGCCACCCCTTCCCT  
CCTTCCCCGCGTCCCCGCGCTCGCCGGCCAGTCAGCTTGCCGGGTTGCTGCCCCGCGAAACCCCGAGGTACCA  
GCCCCGCGCCTCTGCTTCCCTGGGCGCGCGCGCCGCTCCACGCCCTCCTTCTCCCTGGCCCCGGCGCCTGGCACC  
GGGGACCCTTGCTGACGCGAGGCCAGCTCTACTTTTCGCCCCGCGTCTCCTCCGCTGCTCGCCTCTTCCAC  
CAACTCCAACCTCTTCTCCCTCCAGCTCCACTCGCTAGTCCCCGACTCCGCCAGCCCTCGGCCCCGCTGCCGTAG  
CGCCGCTTCCCGTCCGGTCCCAAAGGTGGGAACGCGTCCGCCCGCGCCCGCACC**ATG**GCACGGTTCGGCTTGCC  
CGCGCTTCTCTGCACCCTGGCAGTGCTCAGCGCCGCGCTGCTGGCTGCCGAGCTCAAGTCGAAAAGTTGCTCGG  
AAGTGCAGCGTCTTTACGTGTCCAAAGGCTTCAACAAGAACGATGCCCCCTCCACGAGATCAACGGTGATCAT  
TTGAAGATCTGTCCCAGGGTTCTACCTGCTGCTCTCAAGAGATGGAGGAGAAGTACAGCCTGCAAAGTAAAGA  
TGATTTCAAAGTGTGGTCAGCGAACAGTGCAATCATTTGCAAGCTGTCTTTGCTTCACGTTACAAGAAGTTTG  
ATGAATTTCTCAAAGAACTACTTGAAAATGCAGAGAAATCCCTGAATGATATGTTTGTGAAGACATATGGCCAT  
TTATACATGCAAATTTCTGAGCTATTTAAAGATCTCTTCGTAGAGTTGAAACGTTACTACGTGGTGGGAAATGT  
GAACCTGGAAGAAATGCTAAATGACTTCTGGGCTCGCCTCCTGGAGCGGATGTTCCGCTGGTGAACCTCCAGT  
ACCACTTTACAGATGAGTATCTGGAATGTGTGAGCAAGTATACGGAGCAGCTGAAGCCCTTCGGAGATGTCCCT  
CGCAAATTGAAGCTCCAGGTTACTCGTGCTTTTGTAGCAGCCCGTACTTTGCTCAAGGCTTAGCGGTTGCGGG  
AGATGTGCTGAGCAAGGTCTCCGTGGTAAACCCACAGCCAGTGTACCCATGCCCTGTTGAAGATGATCTACT  
GCTCCCACTGCCGGGGTCTCGTGACTGTGAAGCCATGTTACAACACTGCTCAAACATCATGAGAGGCTGTTTG  
GCCAACCAAGGGGATCTCGATTTTGAATGGAACAATTTCATAGATGCTATGCTGATGGTGGCAGAGAGGCTAGA  
GGGTCCTTTCAACATTGAATCGGTTCATGGATCCCATCGATGTGAAGATTTCTGATGCTATTATGAACATGCAGG  
ATAATAGTGTTCAGTGTCTCAGAAGGTTTCCAGGGATGTGGACCCCCCAAGCCCTCCAGCTGGACGAATT  
TCTCGTTCCATCTCTGAAAGTGCCTTCAGTGCTCGCTTCAGACCACATCACCCCGAGGAACGCCCAACACAGC  
AGCTGGCACTAGTTTGGACCGACTGGTTACTGATGTCAAGGAGAACTGAAACAGGGCCAAGAAATTTCTGGTCCT  
CCCTTCCGAGCAACGTTTGAACGATGAGAGGATGGCTGCAGGAAACGGCAATGAGGATGACTGTTGGAATGGG  
AAAGGCAAAAGCAGGTACCTGTTTGAGTGACAGGAAATGGATTAGCCAACCAGGGCAACAACCCAGAGGTCCA  
GGTTGACACCAGCAAACCAGACATACTGATCCTTCGTCAAATCATGGCTCTTCGAGTGATGACCAGCAAGATGA  
AGAATGCATACAATGGGAACGACGTGGACTTCTTTGATATCAGTGATGAAAGTAGTGGAAGGAAGTGAAGT  
GGCTGTGAGTATCAGCAGTGCCCTTCAGAGTTTGACTACAATGCCACTGACCATGCTGGGAAGAGTGCCAATGA  
GAAAGCCGACAGTGCTGGTGTCCGTCTGGGGCACAGGCCTACCTCCTCACTGTCTTCTGCATCTTGTTCCTGG  
TTATGCAGAGAGAGTGGAGAT**TAA**TTCTCAAACCTCTGAGAAAAAGTGTTATCAAAAAGTTAAAAGGCACCAAGTT  
ATCACTTTTCTACCATCCTAGTGACTTTGCTTTTTTAAATGAATGGACAACAATGTACAGTTTTTACTATGTGGC  
CACTGGTTTAAGAAGTGCTGACTTTGTTTTCTCATTAGTTTTGGGAGGAAAAGGGACTGTGCATTGAGTTGGT  
TCCTGCTCCCCCAAACCATGTTAAACGTGGCTAACAGTGTAGGTACAGAACTATAGTTAGTTGTGATTTGTGA  
TTTTATCACTCTATTATTTGTTTGTATGTTTTTTCTCATTTCGTTTGTGGGTTTTTTTTTCCAAGTGTGATCT  
CGCCTTGTTTTCTTACAAGCAAACCAGGGTCCCTTCTTGGCACGTAACATGTACGTATTTCTGAAATATTAAATA  
GCTGTACAGAAGCAGGTTTTATTATCATGTTATCTTATTAAGAAAAAGCCCCAAAAGC

97/330

**FIGURE 97**

MARFGLPALLCTLAVLSAALLAAELKSKSCSEVRRLYVSKGFNKNDAPLHEINGDHLKICPQ  
GSTCCSQEMEKEYSLQSKDDFKSVVSEQCNHLQAVFASRYKKFDEFFKELLENAEKSLNDMF  
VKTYGHLQNSSELFKDLFVELKRYVVGNNLEEMLNDFWARLLERMFRVNSQYHFTDEY  
LECVSKYTEQLKPFQDVPRKLKLQVTRAFVAARTFAQGLAVAGDVVSKVSVVNPTAQCTHAL  
LKMIYCSHCRGLVTVKPCYNYCSNIMRGCLANQGDLD FEWNNFIDAMLMVAERLEGPFNIES  
VMDPIDVKISDAIMNMQDNSVQVSQKVFQGC GPPKPLPAGRISR SISESAFSARFRPHHPEE  
RPTTAAGTSLDRLVTDVKEKLKQAKKFWSSLPSNVCNDERMAAGNGNEDDCWNGKGKSR YLF  
AVTGNGLANQGNNPEVQVDTSKPDILILRQIMALRVMTSKMKNAYNGNDVDFDISDESSGE  
GSGSGCEYQQCPSEFDYNATDHAGKSANEKADSAGVRPGAQAYLLTVFCILFLVMQREWR

98/330

**FIGURE 98**

CTCGCCCTCAAATGGGAACGCTGGCCTGGGACTAAAGCATAGACCACCAGGCTGAGTATCCT  
GACCTGAGTCATCCCCAGGGATCAGGAGCCTCCAGCAGGGAACCTTCCATTATATTCTTCAA  
GCAACTTACAGCTGCACCGACAGTTGCG**ATG**AAGTTCTAATCTCTTCCCTCCTCCTGTTGC  
TGCCACTAATGCTGATGTCCATGGTCTCTAGCAGCCTGAATCCAGGGGTCGCCAGAGGCCAC  
AGGGACCGAGGCCAGGCTTCTAGGAGATGGCTCCAGGAAGGCGGCCAAGAATGTGAGTGCAA  
AGATTGGTTCCTGAGAGCCCCGAGAAGAAAATTCATGACAGTGTCTGGGCTGCCAAAGAAGC  
AGTGCCCTGTGATCATTTCAAGGGCAATGTGAAGAAAACAAGACACCAAAGGCACCACAGA  
AAGCCAAACAAGCATTCCAGAGCCTGCCAGCAATTTCTCAAACAATGTCAGCTAAGAAGCTT  
TGCTCTGCCTTTG**TAG**GAGCTCTGAGCGCCCACTCTTCCAATTAAACATTCTCAGCCAAGAA  
GACAGTGAGCACACCTACCAGACACTCTTCTTCTCCACCTCACTCTCCCACTGTACCCACC  
CCTAAATCATTCAGTGCTCTCAAAAAGCATGTTTTTCAAGATCATTTTGTTTGTTGCTCTC  
TCTAGTGTCTTCTTCTCTCGTCAGTCTTAGCCTGTGCCCTCCCCTTACCCAGGCTTAGGCTT  
AATTACCTGAAAGATTCCAGGAAACTGTAGCTTCCTAGCTAGTGTCATTTAACCTTAAATGC  
AATCAGGAAAGTAGCAAACAGAAAGTCAATAAATATTTTTTAAATGTCAAAAAAAAAAAAAAAAAA

99/330

**FIGURE 99**

MKVLISSLLLLLPLMLMSMVSSSLNPGVARGHRDRGQASRRWLQEGGQECECKDWFLRAPRR  
KFMTVSGLPKKQCPDHFKGNVKKTRHQRHHRKPNKHSRACQQFLKQCQLRSFALPL



100/330

**FIGURE 100**

A**ATG**GCTGTCTTAGTACTTCGCCTGACAGTTGTCCTGGGACTGCTTGTCTTATTCCTGACCT  
GCTATGCAGACGACAAACCAGACAAGCCAGACGACAAGCCAGACGACTCGGGCAAAGACCCA  
AAGCCAGACTTCCCCAAATTCCTAAGCCTCCTGGGCACAGAGATCATTGAGAATGCAGTCGA  
GTTTCATCCTCCGCTCCATGTCCAGGAGCACAGGATTTATGGAATTTGATGATAATGAAGGAA  
AACATTCATCAAAG**TGA**CATCCTCAGGACACACCCATGTGGCTCCTGGACAATCCAAGAGCA  
GCCAAATCCTGCTTTTCCAGTTTGGCTCCACAAGTCCTCCAGGACAGAGCCCTCAAAGCAAC  
TCCCAACGAGTTCTCAGGATTCAGGCTCTGGCTTCAACCAAACAGAACTCATTTTGAACACC  
CTGACTGCATTTTTGCTTTTAGAAAGTTAGAATAAATATGGCGCTTTGGGATCACATAGTTG  
ATGGAGAGGAAA

101/330

**FIGURE 101**

MAVLVLRLTVVLGLLVFLTCYADDKPDKPDDKPDDSGKDPKPDFPKFLSLLGTEIIENAVE  
FILRSMRSTGFMEFDDNEGKHSSK

102/330

**FIGURE 102**

GGACGCCAGCGCCTGCAGAGGCTGAGCAGGGAAAAAGCCAGTGCCCCAGCGGAAGCACAGCT  
CAGAGCTGGTCTGCC**ATG**GACATCCTGGTCCCACCTCCTGCAGCTGCTGGTGCTGCTTCTTAC  
CCTGCCCCCTGCACCTCATGGCTCTGCTGGGCTGCTGGCAGCCCCCTGTGCAAAGCTACTTCC  
CCTACCTGATGGCCGTGCTGACTCCCAAGAGCAACCGCAAGATGGAGAGCAAGAAACGGGAG  
CTCTTCAGCCAGATAAAGGGGCTTACAGGAGCCTCCGGGAAAGTGGCCCTACTGGAGCTGGG  
CTGCGGAACCGGAGCCAACTTTTCAGTTCTACCCACCGGGCTGCAGGGTCACCTGCCTAGACC  
CAAATCCCCACTTTGAGAAGTTCTTGACAAAGAGCATGGCTGAGAACAGGCACCTCCAATAT  
GAGCGGTTTGTGGTGGCTCCTGGAGAGGACATGAGACAGCTGGCTGATGGCTCCATGGATGT  
GGTGGTCTGCACTCTGGTGCTGTGCTCTGTGCAGAGCCCAAGGAAGGTCCTGCAGGAGGTCC  
GGAGAGTACTGAGACCGGGAGGTGTGCTCTTTTTCTGGGAGCATGTGGCAGAACCATATGGA  
AGCTGGGCCTTCATGTGGCAGCAAGTTTTTCGAGCCCACCTGGAAACACATTGGGGATGGCTG  
CTGCCTCACCAGAGAGACCTGGAAGGATCTTGAGAACGCCCAGTTCTCCGAAATCCAAATGG  
AACGACAGCCCCCTCCCTTGAAGTGGCTACCTGTTGGGCCCCACATCATGGGAAAGGCTGTC  
AAACAATCTTTCCCAAGCTCCAAGGCACTCATTTGCTCCTTCCCCAGCCTCCAATTAGAACA  
AGCCACCCACCAGCCTATCTATCTTCCACTGAGAGGGACCT**TAG**CAGAATGAGAGAAGACATT  
CATGTACCACCTACTAGTCCCTCTCTCCCCAACCTCTGCCAGGGCAATCTCTAACTTCAATC  
CCGCCTTCGACAGTGAAAAAGCTCTACTTCTACGCTGACCCAGGGAGGAAACACTAGGACCC  
TGTTGTATCCTCAACTGCAAGTTTCTGGACTAGTCTCCCAACGTTTGCCTCCCAATGTTGTC  
CCTTTCCTTCGTTCCCATGGTAAAGCTCCTCTCGCTTTCCTCCTGAGGCTACACCCATGCGT  
CTCTAGGAACTGGTCACAAAAGTCATGGTGCCTGCATCCCTGCCAAGCCCCCTGACCCTCT  
CTCCCCACTACCACCTTCTTCTGAGCTGGGGGCACCAGGGAGAATCAGAGATGCTGGGGAT  
GCCAGAGCAAGACTCAAAGAGGCAGAGGTTTTGTTCTCAAATATTTTTTAATAAATAGACGA  
AACCACG

103/330

**FIGURE 103**

MDILVPLLQLLVLLLTLP LHL MALLGCWQPLCKSYFPYLM AVLTPKSNRKMESKKRELF S Q I  
KGLTGASGKVALLELGCGTGANFQFYPPGCRVTCLDPNPHFEKFLTKSMAENRHLQYERFVV  
APGEDMRQLADGSMDVVVCTLVLC SVQSPRKVLQEVRRLRPGGV LFFWEHVAEPYGSWAFM  
WQQVFEPTWKHIGDGCCLTRETWKDLENAQFSEIQMERQPPPLKWLPVGPHIMGKAVKQSFP  
SSKALICSFPSLQLEQATHQPIYLPLRGT

104/330

**FIGURE 104**

GTGGGATTTATTTGAGTGCAAGATCGTTTTCTCAGTGGTGGTGGAAAGTTGCCTCATCGCAGG  
CAGATGTTGGGGCTTTGTCCGAACAGCTCCCCCTCTGCCAGCTTCTGTAGATAAGGGTTAAAA  
ACTAATATTTATATGACAGAAGAAAAAG**ATG**CATTCCGTAAAGTAAACATCATCATCTTGG  
TCCTGGCTGTTGCTCTCTTCTTACTGGTTTTGCACCATAACTTCCTCAGCTTGAGCAGTTTG  
TTAAGGAATGAGGTTACAGATTGAGGAATTGTAGGGCCTCAACCTATAGACTTTGTCCCAA  
TGCTCTCCGACATGCAGTAGATGGGAGACAAGAGGAGATTCTGTGGTCATCGCTGCATCTG  
AAGACAGGCTTGGGGGGGCCATTGCAGCTATAAACAGCATTGAGCACAACACTCGCTCCAAT  
GTGATTTTCTACATTGTTACTCTCAACAATACAGCAGACCATCTCCGGTCTGGCTCAACAG  
TGATTCCCTGAAAAGCATCAGATACAAAATTGTCAATTTTGACCCTAAACTTTTGGAAGGAA  
AAGTAAAGGAGGATCCTGACCAGGGGGAATCCATGAAACCTTTAACCTTTGCAAGGTTCTAC  
TTGCCAATTCTGGTTCCCAGCGCAAAGAAGGCCATATACATGGATGATGATGTAATTGTGCA  
AGGTGATATTCTTGCCCTTTACAATACAGCACTGAAGCCAGGACATGCAGCTGCATTTTCAG  
AAGATTGTGATTGAGCCTCTACTAAAGTTGTCATCCGTGGAGCAGGAAACAGTACAATTAC  
ATTGGCTATCTTGACTATAAAAAGGAAAGAATTTCGTAAGCTTTCCATGAAAGCCAGCACTTG  
CTCATTTAATCCTGGAGTTTTTTGTTGCAAACCTGACGGAATGGAAACGACAGAATATAACTA  
ACCAACTGGAAAAATGGATGAAACTCAATGTAGAAGAGGGACTGTATAGCAGAACCTGGCT  
GGTAGCATCACAAACACCTCCTCTGCTTATCGTATTTTATCAACAGCACTCTACCATCGATCC  
TATGTGGAATGTCCGCCACCTTGGTTCCAGTGCTGGAAAACGATATTCACCTCAGTTTGTA  
AGGCTGCCAAGTTACTCCATTGGAATGGACATTTGAAGCCATGGGGAAGGACTGCTTCATAT  
ACTGATGTTTGGGAAAAATGGTATATTCCAGACCCAACAGGCAAATTCAACCTAATCCGAAG  
ATATACCGAGATCTCAAACATAAAG**TGA**AACAGAATTTGAACTGTAAGCAAGCATTCTCAG  
GAAGTCCTGGAAGATAGCATGCATGGGAAGTAACAGTTGCTAGGCTTCAATGCCTATCGGTA  
GCAAGCCATGGAAAAAGATGTGTCAGCTAGGTAAAGATGACAACTGCCCTGTCTGGCAGTC  
AGCTTCCCAGACAGACTATAGACTATAAATATGTCTCCATCTGCCTTACCAAGTGTTTTCTT  
ACTACAATGCTGAATGACTGGAAAGAAGAACTGATATGGCTAGTTCAGCTAGCTGGTACAGA  
TAATTCAAACTGCTGTTGGTTTTAATTTTGTAACCTGTGGCCTGATCTGTAAATAAACTT  
ACATTTTTC

105/330

**FIGURE 105**

MSFRKVNIIILVLAVALFLLVLHHNFLSLSSLLRNEVTDSGIVGPQPIDFVPNALRHAVDGR  
QEEIPVVIAASEDRLGGAIAAINSIQHNTSRNVIFYIVTLNNTADHLRSWLNSDSLKSIRYK  
IVNFDPKLLEGKVKEDPDQGESMKPLTFARFYLPILVPSAKKAIYMDDDVIVQGDILALYNT  
ALKPGHAAAFSEDCDSASTKVVIRGAGNQYNYIGYLDYKKERIRKLSMKASTCSFNPGVFVA  
NLTEWKRQNI TNQLEKWMKLNVEEGLYSRTLGSITTPPLLIVFYQQHSTIDPMWNVRLHLS  
SAGKRYSPQFVKAALLHWNGHLKPWGRTASYTDVWEKWYIPDPTGKFNLIRRYTEISNIK

106/330

**FIGURE 106**

TGGTTTTTGCCCCATAAATTCCTCAGCTTGAGCAGTTTGTTAAGGAATGAGGTTACAGATT  
CAGGAATTNTAGGNCCTCAACCTNTAGANTTTGTCCCAAATGTTCTCCGACATGCAGTAGAT  
GGGAGACAAGAGGAGATTCTGTGGTCATCGCTGCATNTGAAGACAGGCTTGGGGGGGCCAT  
TGCAGCTATAAACAGCATTTCAGCACAACACTCGNTCCAATGTGATTTTCTACATTGTTACTC  
TCAACAATACAGCAGACCATNTCCGGTCCTGGNTCAACAGTGATTCCCTGAAAAGCATCAGA  
TACAAAATTGTCAATTTTGACCCTAACTTTTGGAAGGAAAAGTAAAGGAGGATCCTGACCA  
GGGGGAATCCATGAAACCTTTAACCTTTGCAAGGTTCTACTTGCCAATTCTGGTTCCCAGCG  
CAAAGAAGGCCATATACATGGATGATGATGTAATTGTGCAAGGTGATATTCTTGCCCTTTAC  
AATACAGCACTGAAGCCAGGACATGCAGCTGCATTTTCAGAAGATTGTGATTCAGCCTCTAC  
TAAAGTTGTCATCCGTGGAGCAGGAAA

107/330

**FIGURE 107**

CGACGCTCTAGCGGTTACCGCTGCGGGCTGGCTGGGCGTAGTGGGGCTGCGCGGCTGCCACG  
GAGCTAGAGGGCAAGTGTGCTCGGCCCAGCGTGCAGGGAACGCGGGCGGCCAGACAACGGGC  
TGGGCTCCGGGGCCTGCGGCGCGGGCGCTGAGCTGGCAGGGCGGGTCGGGGCGCGGGCTGCA  
TCCGCATCTCCTCCATCGCCTGCAGTAAGGGCGGCCGCGGCGAGCCTTTGAGGGGAACGACT  
TGTCGGAGCCCTAACCAGGGGTGTCTCTGAGCCTGGTGGGATCCCCGGAGCGTCACATCACT  
TTCCGATCACTTCAAAGTGGTTAAAACTAATATTTATATGACAGAAGAAAAAGATGTCATT  
CCGTAAAGTAAACATCATCATCTTGGTCTGGGCTGTTGCTCTCTTCTTACTGGTTTTTGCAC  
CATAACTTCCTCAGCTTGAGGCAGTTTGTTAAGGAATGAGGTTACAGATTCAGGAATTGTAG  
GGCCTCAACCTATAGGACTTTGTCCCAAATGCTCTCCGACATGCAGTAGATGGGAGACAAGA  
GGAGATTCCTGTGGTCATCGCTGCATCTGAAGACAGGCTTGGGGGGGCCATTGCAGCTATAA  
ACAGCATTCAGCACAACACTCGCTCCAATGTGATTTTCTACATTGTTACTCTCAACAATACA  
GCAGACCATCTCCGGTCCTGGGCTCAACAGTGATTCCCTGAAAAGCATCAGATACAAAATTG  
TCAATTTTGACCCTAACTTTTGAAGGAAAAGTAAAGGAGGATCCTGACCAGGGGGAATCC  
ATGAAACCTTTAACCTTTGCAAGGTTCTACTTGCCAATTCTGGGTTCCCAGCGCAAAGAAGG  
CCATATACATGGATGATGATGTAATTGTGCAAGGTGATATTCTTGCCCTTTACAATACAGCA  
CTGAAGCCAGGACATGCAGCTGCATTTTTCAGAAGATTGTGATTCAGCCTCTACTAAAGTTGT  
CATCCGTGGAGCAGGAAACCAGTACAATTACATTGGCTATCTTGACTATAAAAAGGAAAGAA  
TTCGTAAGCTTTCCATGAAAGCCAGCACTTGCTCATTTAATCCTGGAGTTTTTGTGCAAAC  
CTGACGGAATGGAAACGACAGAATATACTAACCAACTGGAAAAATGGATGAACTCAATGT  
AGAAGAGGGACTGTATAGCAGAACCCTGGCTGGTAGCATCACAAACACCTCCTCTGCTTATCG  
TATTTTATCAACAGCACTCTACCATCGATCCTATGTGGAATGTCCGCCACCTTGGTTCCAGT  
GCTGGAAAACGATATTCACCTCAGTTTGTAAAGGCTGCCAAGTTACTCCATTGGAATGGACA  
TTTGAAGCCATGGGGAAGGACTGCTTCATATACTGATGTTTGGGGAAAAATGGTATATTCCA  
GACCCAACAGGCAAATTCAACCTAATCCGAAGATATACCGAGATCTCAAACATAAAGTGAAA  
CAGAATTTGAACTGTAAGCAAGCATTTCTCAGGAAGTCCTGGAAGATAGCATGCGTGGGAAG  
TAACAGTTGCTAGGCTTCAATGCCTATCGGTAGCAAGCCATGGAAAAAGATGTGTCAGCTAG  
GTAAAGATGACAACTGCCCTGTCTGGCAGTCAGCTTCCCAGACAGACTATAGACTATAAAT  
ATGTCTCCATCTGCCTTACCAAGTGTTTTCTTACTACAATGCTGAATGACTGGAAAGAAGAA  
CTGATATGGCTAGTTCAGCTAGCTGGTACAGATAATTCAAAACCTGCTGTTGGTTTTAATTTT  
GTAACCTGTGGCCTGATCTGTAAATAAACTTACATTTTTTCAATAGGTAAAAA



108/330

**FIGURE 108**

CTGCAGGTAGACATCTCCACTGCCCAGGAATCACTGAGCGTGCAGACAGCACAGCCTCCTCT  
GAAGGCCGGCCATACCAGAGTCCTGCCTCGGCATGGGCCTCACCATTGAGGCAGCTCCACTG  
TCTGTGCTGGTCTGAGGGTGTGCTGCCTGTC**ATG**GGGGGCAGCCATCTCCCAGGGGGCCCTCATC  
GCCATCGTCTGCAACGGTCTCGTGGGCTTCTTGCTGCTGCTGCTCTGGGTCATCCTCTGCTG  
GGCCTGCCATTCTCGTCTGCCGACGTTGACTCTCTCTCTGAATCCAGTCCCAACTCCAGCCC  
TGGCCCCTGTCCTGAGAAGGCCCCACCACCCAGAAAGCCCAGCCATGAAGGCAGCTACCTGC  
TGCAGCCCTGAAGGCCCCCTGGCCTAGCCTGGAGCCCAGGACC**TAA**GTCCACCTCACCTAGAG  
CCTGGAATTAGGATCCCAGAGTTCAGCCAGCCTGGGGTCCAGAACTCAAGAGTCCGCCTGCT  
TGGAGCTGGACCCAGCGGGCCAGAGTCTAGCCAGCTTGGCTCCAATAGGAGCTCAGTGGCCC  
TAAGGAGATGGGCCTGGGGTGGGGGCTTATGAGTTGGTGCTAGAGCCAGGGCCATCTGGACT  
ATGCTCCATCCCAAGGGCCAAGGGTCAGGGGGCCGGGTCCACTCTTTCCCTAGGCTGAGCACC  
TCTAGGCCCTCTAGGTTGGGGAAGCAAACCTGGAACCCATGGCAATAATAGGAGGGTGTCCAG  
GCTGGGCCCCCTCCCCTGGTCCTCCCAGTGTTGCTGGATAATAAATGGAACCTATGGCTCTAA  
AAAAAAAAAAAAAAAAAAAA

109/330

**FIGURE 109**

MGA AISQ GALIA IVCNGLVG FLLLLLWVILCWACHSRLPTLTSLNPVPTPALAPVLRRPHH  
PRSPAMKAATCCSPEGPWPSLEPRT

110/330

**FIGURE 110**

GTTTGAATTCCTTCAACTATACCCACAGTCCAAAAGCAGACTCACTGTGTCCCAGGCTACCA  
GTTCCCTCCAAGCAAGTCATTTCCCTTATTTAACCGATGTGTCCCTCAAACACCTGAGTGCTA  
CTCCCTATTTGCATCTGTTTTGATAAATGATGTTGACACCCTCCACCGAATTCTAAGTGGA  
TC**ATG**TCGGGAAGAGATACAATCCTTGGCCTGTGTATCCTCGCATTAGCCTTGTCTTTGGCC  
ATGATGTTTACCTTCAGATTCATCACCACCCTTCTGGTTCACATTTTCATTTCAATTGGTTAT  
TTTGGGATTGTTGTTTGTCTGCGGTGTTTTATGGTGGCTGTATTATGACTATACCAACGACC  
TCAGCATAGAATTGGACACAGAAAGGGAAAATATGAAGTGCGTGCTGGGGTTTGCTATCGTA  
TCCACAGGCATCACGGCAGTGCTGCTCGTCTTGATTTTTGTTCTCAGAAAGAGAATAAAATT  
GACAGTTGAGCTTTTCCAAATCACAAATAAAGCCATCAGCAGTGCTCCCTTCCTGCTGTTCC  
AGCCACTGTGGACATTTGCCATCCTCATTTTCTTCTGGGTCCCTCTGGGTGGCTGTGCTGCTG  
AGCCTGGGAAGTGCAGGAGCTGCCCAGGTTATGGAAGGCGCCAAGTGGAATATAAGCCCCT  
TTCGGGCATTTCGGTACATGTGGTTCGTACCATTTAATTGGCCTCATCTGGACTAGTGAATTCA  
TCCTTGCGTGCCAGCAAATGACTATAGCTGGGGCAGTGGTTACTTGTTATTTCAACAGAAGT  
AAAAATGATCCTCCTGATCATCCCATCCTTTCGTCTCTCTCCATTCTCTTCTTCTACCATCA  
AGGAACCGTTGTGAAAGGGTCATTTTTAATCTCTGTGGTGAGGATTCCGAGAATCATTGTCA  
TGTACATGCAAACGCACTGAAAGAACAGCAGCATGGTGCATTGTCCAGGTACCTGTTCCGA  
TGCTGCTACTGCTGTTTCTGGTGTCTTGACAAATACCTGCTCCATCTCAACCAGAATGCATA  
TACTACAACCTGCTATTAATGGGACAGATTTCTGTACATCAGCAAAGATGCATTCAAATCT  
TGTCCAAGAACTCAAGTCACTTTACATCTATTAAGTCTTTGGAGACTTCATAATTTTTCTA  
GGAAAGGTGTTAGTGGTGTGTTTCACTGTTTTTGGAGGACTCATGGCTTTTAACTACAATCG  
GGCATTCCAGGTGTGGGCAGTCCCTCTGTTATTGGTAGCTTTTTTTGCCTACTTAGTAGCCC  
ATAGTTTTTTTATCTGTGTTTGAAACTGTGCTGGATGCACTTTTCCTGTGTTTTGCTGTTGAT  
CTGGAAACAAATGATGGATCGTCAGAAAAGCCCTACTTTATGGATCAAGAATTTCTGAGTTT  
CGTAAAAAGGAGCAACAAATTAAACAATGCAAGGGCACAGCAGGACAAGCACTCATTAAGGA  
ATGAGGAGGGAACAGAACTCCAGGCCATTGTGAGA**TAG**ATACCCATTTAGGTATCTGTACCT  
GGAAAACATTTCTTCTAAGAGCCATTTACAGAATAGAAGATGAGACCACTAGAGAAAAGTT  
AGTGAATTTTTTTTTTAAAAGACCTAATAAACCTATTCTTCCTCAAAA

111/330

**FIGURE 111**

MSGRDTILGLCILALALSLAMMFTFRFITTTLLVHIFISLVILGLLFVCGVLWWLYDYTNDL  
SIELDTERENMKCVLGFAIVSTGITAVLLVLI FVLRKRIKLTVELFQITNKAISSAPFLLFQ  
PLWTFAILIFFWVLWVAVLLSLGTAGAAQVMEGGQVEYKPLSGIRYMWSYHLIGLIWTSEFI  
LACQQMTIAGAVVTCYFNRSKNDPPDHPILSSLSILFFYHQGTVVKGSFLISVVRIPRIIVM  
YMQNALKEQQHGALSRYLFRCCYCCFWCLDKYLLHLNQNAYTTTAINGTDFCTSAKDAFKIL  
SKNSSHFTSINCFGDFIIFLGKVLVVCFTVFGGLMAFNYNRAFQVWAVPLLLVAFFAYLVAH  
SFLSVFETVLDALFLCFAVDLETNDGSSEKPYFMDQEFLSFVKRSNKLNNARAQQDKHSLRN  
EEGTELQAIVR

**FIGURE 112**

[illegible]

113/330

**FIGURE 113**

MRTVVLTMKASVIEMFLVLLVTGVHSNKETAKKIKRPKFTVPQINCDVKAGKIIDPEFIVKC  
PAGCQDPKYHVGTDVYASYSSVCGAAVHSGVLDNSGGKILVRKVAGQSGYKGSYSNGVQSL  
SLPRWRESFIVLESKPKKGVTPSALTYSSSKSPAAQAGETTKAYQRPPIPGTTAQPVTLMQ  
LLAVTVAVATPTTLPRPSPSAASTTSIPRPQSVGHRSEQEMDLWSTATYTSSQNRPRADPGIQ  
RQDPGGAAFQKPVGADVSLGLVPKEELSTQSLPVS LGDPNCKIDLSFLIDGSTSIGKRRFR  
IQKQLLADVAQALDIGPAGPLMGVVQYGDNPATHFNLKTHNTSRDLKTAIEKITQRGGLSNV  
GRAISFVTKNFFSKANGNRSGAPNVVVVMVDGWPTDKVEEASRLARESGINIFFITIEGAAE  
NEKQYVVEPNFANKAVCRTNGFYSLHVQSWFGLHKTQLPLVKRVCDTDRLACSKTCLNSADI  
GFVIDGSSSVGTGNFRTVLQFVTNLTKEFEISD TDTRIGAVQYTYEQRLEFGFDKYSSKPD  
LNAIKRVGYWSGGTSTGAAINFALEQLFKKSKPNKRKLMILITDGRSYDDVRI PAMAAHLKG  
VITYAIGVAWAAQEELEVIATHPARDHSFFVDEFDNLHQYVPRIIQNICTEFNSQPRN

114/330

**FIGURE 114**

CAGGATGAACTGGTTGCAGTGGCTGCTGCTGCTGCTGCGGGGGCGCTGAGAGGACACGAGCTCTA  
TGCCTTTCCGGCTGCTCATCCCGCTCGGCCTCCTGTGCGCGCTGCTGCCTCAGCACCATGGT  
GCGCCAGGTCCCGACGGCTCCGCGCCAGATCCCGCCCACTACAGTTTTTCTCTGACTCTAAT  
TGATGCACTGGACACCTTGCTGATTTTGGGGAATGTCTCAGAATTCCAAAGAGTGGTTGAAG  
TGCTCCAGGACAGCGTGGACTTTGATATTGATGTGAACGCCTCTGTGTTTGAAACAAACATT  
CGAGTGGTAGGAGGACTCCTGTCTGCTCATCTGCTCTCCAAGAAGGCTGGGGTGGAAGTAGA  
GGCTGGATGGCCCTGTTCCGGGCCTCTCCTGAGAATGGCTGAGGAGGCGGCCCGAAAACCTCC  
TCCCAGCCTTTCAGACCCCCACTGGCATGCCATATGGAACAGTGAACTTACTTCATGGCGTG  
AACCCAGGAGAGACCCCTGTCACCTGTACGGCAGGGATTGGGACCTTCATTGTTGAATTTGC  
CACCTGAGCAGCCTCACTGGTGACCCGGTGTTTGAAGATGTGGCCAGAGTGGCTTTGATGC  
GCCTCTGGGAGAGCCGGTCAGATATCGGGCTGGTGGCAACCACATTGATGTGCTCACTGGC  
AAGTGGGTGGCCCAGGACGCAGGCATCGGGGCTGGCGTGGACTCCTACTTTGAGTACTTGGT  
GAAAGGAGCCATCCTGCTTCAGGATAAGAAGCTCATGGCCATGTTCTTAGAGTATAACAAAG  
CCATCCGGAACCTACACCCGCTTCGATGACTGGTACCTGTGGGTTCAGATGTACAAGGGGACT  
GTGTCCATGCCAGTCTTCCAGTCCTTGGAGGCCTACTGGCCTGGTCTTCAGAGCCTCATTGG  
AGACATTGACAATGCCATGAGGACCTTCCTCAACTACTACACTGTATGGAAGCAGTTTGGGG  
GGCTCCCGGAATTCTACAACATTCTCAGGGATACACAGTGGAGAAGCGAGAGGGCTACCCA  
CTTCGGCCAGAACTTATTGAAAGCGCAATGTACCTCTACCGTGCCACGGGGGATCCCACCCT  
CCTAGAACTCGGAAGAGATGCTGTGGAATCCATTGAAAAAATCAGCAAGGTGGAGTGCGGAT  
TTGCAACAATCAAAGATCTGCGAGACCACAAGCTGGACAACCGCATGGAGTCGTTCTTCCTG  
GCCGAGACTGTGAAATACCTCTACCTCCTGTTTGACCCAACCAACTTCATCCACAACAATGG  
GTCCACCTTCGACGCGGTGATCACCCCTATGGGGAGTGCATCCTGGGGGCTGGGGGGTACA  
TCTTCAACACAGAAGCTCACCCCATCGACCTTGCCGCCCTGCACTGCTGCCAGAGGCTGAAG  
GAAGAGCAGTGGGAGGTGGAGGACTTGATGAGGGAATTCTACTCTCTCAAACGGAGCAGGTC  
GAAATTTTCAAAAAACACTGTTAGTTCGGGGCCATGGGAACCTCCAGCAAGGCCAGGAACAC  
TCTTCTCACCAGAAAACCATGACCAGGCAAGGGAGAGGAAGCCTGCCAAACAGAAGGTCCCA  
CTTCTCAGCTGCCCCAGTCAGCCCTTACCTCCAAGTTGGCATTACTGGGACAGGTTTTCT  
AGACTCCTCATAACCACTGGATAATTTTTTTATTTTTATTTTTTTGAGGCTAAACTATAATA  
AATTGCTTTTGGCTATCATAAAA

115/330

**FIGURE 115**

MPFRLLIPLGLLCALLPQHHGAPGPDGSAPDPAHYSFSLTLIDALDTLLILGNVSEFQRVVE  
VLQDSVDFDIDVNASVFETNIRVVGGLLSAHLLSKKAGVEVEAGWPCSGPLLRMAEEAARKL  
LPAFQTPTGMPYGTVNLLHGVNPGETPVTCTAGIGTFIVEFATLSSLTGDPVFEDVARVALM  
RLWESRSDIGLVGNHIDVLTGKWVAQDAGIGAGVDSYFEYLVKGAILLQDKKLMAMFLEYNK  
AIRNYTRFDDWYLWVQMYKGTVSMPVFQSLEAYWPGLQSLIGDIDNAMRTFLNYYTVWKQFG  
GLPEFYNI PQGYTVEKREGYPLRPELIESAMYLYRATGDPTLLELGRDAVESIEKISKVECG  
FATIKDLRDHKL DNRMESFFLAETVKYLYLLFDPTNFIHNNGSTFDAVITPYGECILGAGGY  
IFNTEAHPIDLAALHCCQRLKEEQWEVEDLMREFYSLKRSRSKFQKNTVSSGPWEPPARPGT  
LFSPENHDQARERKPAKQKVPLLSCPSQPFTSKLALLGQVFLDSS



116/330

**FIGURE 116**

AAAGTTACATTTTCTCTGGAACCTCCTAGGCCACTCCCTGCTGATGCAACATCTGGGTTTG  
GGCAGAAAGGAGGGTGCTTCGGAGCCCGCCCTTTCTGAGCTTCCTGGGCCGGCTCTAGAACA  
ATTCAGGCTTCGCTGCGACTCAGACCTCAGCTCCAACATATGCATTCTGAAGAAAGATGGCT  
GAGATGGACAGAATGCTTTATTTTGGAAAGAAACAATGTTCTAGGTCAAACCTGAGTCTACCA  
**AATG**CAGACTTTCACAATGGTTCTAGAAGAAATCTGGACAAGTCTTTTCATGTGGTTTTTCT  
ACGCATTGATTCCATGTTTGCTCACAGATG<sup>1</sup>AAGTGGCCATTCTGCCTGCCCCCTCAGAACCTC  
TCTGTACTCTCAACCAACATGAAGCATCTCTTGATGTGGAGCCCAGTGATCGCGCCTGGAGA  
AACAGTGTACTATTCTGTCTGAATACCAGGGGGAGTACGAGAGCCTGTACACGAGCCACATCT  
GGATCCCCAGCAGCTGGTGCTCACTCACTGAAGGTCCTGAGTGTGATGTCACTGATGACATC  
ACGGCCACTGTGCCATACAACCTTCGTGTCAGGGCCACATTGGGCTCACAGACCTCAGCCTG  
GAGCATCCTGAAGCATCCCTTTAATAGAAACTCAACCATCCTTACCCGACCTGGGATGGAGA  
TCACCAAAGATGGCTTCCACCTGGTTATTGAGCTGGAGGACCTGGGGCCCCAGTTTGAGTTC  
CTTGTGGCCTACTGGAGGAGGGAGCCTGGTGCCGAGGAACATGTCAA<sup>2</sup>AATGGTGAGGAGTGG  
GGGTATTCCAGTGCACCTAGAAACCATGGAGCCAGGGGCTGCATACTGTGTGAAGGCCCAGA  
CATTCGTGAAGGCCATTGGGAGGTACAGCGCCTTCAGCCAGACAGAATGTGTGGAGGTGCAA  
GGAGAGGCCATTCCCCTGGTACTGGCCCTGTTTGCCCTTGTTGGCTTCATGCTGATCCTTGT  
GGTCGTGCCACTGTTTCGTCTGGAAAATGGGCCGGCTGCTCCAGTACTCCTGTTGCCCCGTGG  
TGGTCCTCCCAGACACCTTGAAAATAACCAATTCACCCCAGAAGTTAATCAGCTGCAGAAGG  
GAGGAGGTGGATGCCTGTGCCACGGCTGTGATGTCTCCTGAGGAACCTCCTCAGGGCCTGGAT  
CTCA**TAG**GTTTGCGGAAGGGCCCAGGTGAAGCCGAGAACCTGGTCTGCATGACATGGAAACC  
ATGAGGGGACAAGTTGTGTTTCTGTTTTCGCCACGGACAAGGGATGAGAGAAGTAGGAAGA  
GCCTGTTGTCTACAAGTCTAGAAGCAACCATCAGAGGCAGGGTGGTTTGTCTAACAGAACAC  
TGACTGAGGCTTAGGGGATGTGACCTCTAGACTGGGGGCTGCCACTTGCTGGCTGAGCAACC  
CTGGGAAAAGTGACTTCATCCCTTCGGTCCTAAGTTTTCTCATCTGTAATGGGGGAATTACC  
TACACACCTGCTAAACACACACACACAGAGTCTCTCTCTATATATACACACGTACACATAAA  
TACACCCAGCACTTGCAAGGCTAGAGGGAAACTGGTGACACTCTACAGTCTGACTGATTCAG  
TGTTTCTGGAGAGCAGGACATAAATGTATGATGAGAATGATCAAGGACTCTACACACTGGGT  
GGCTTGGAGAGCCCACTTTCCCAGAATAATCCTTGAGAGAAAAGGAATCATGGGAGCAATGG  
TGTTGAGTTCACTTCAAGCCCAATGCCGGTGACAGAGGGGAATGGCTTAGCGAGCTCTACAGT  
AGGTGACCTGGAGGAAGGTCACAGCCACACTGAAAATGGGATGTGCATGAACACGGAGGATC  
CATGAACTACTGTAAAGTGTTGACAGTGTGTGCACACTGCAGACAGCAGGTGAAATGTATGT  
GTGCAATGCGACGAGAATGCAGAAGTCAGTAACATGTGCATGTTTGTGTGCTCCTTTTTTC  
TGTTGGTAAAGTACAGAATTCAGCAAATAAAAAGGGCCACCCTGGCCAAAAGCGGTAAAAAA  
AAAAAAAAAA

117/330

**FIGURE 117**

MQTFTMVLEEIWTSLEFMWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHLMLWSPVIAPGE  
TVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTS  
SILKHPFNRRNSTILTRPGMEITKDGFHLVIELEDLGPQFEFLVAYWRREPGAEEHVKMVRSG  
GIPVHLETMEPGAAYCVKAQTFVKAIGRYSAFSQTECVEVQGEAIPVLALFAFVGFMILIV  
VVPLFVWKMGRLLQYSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVMSPEELLRAWIS

**Important features:****Signal peptide:**

amino acids 1-29

**Transmembrane domain:**

amino acids 230-255

**N-glycosylation sites.**

amino acids 40-43 and 134-137

**Tissue factor proteins homology.**

amino acids 92-119

**Integrins alpha chain protein homology.**

amino acids 232-262

118/330

**FIGURE 118**

TCCTGCTGATGCACATCTGGGTTTGGCAAAAGGAGGTTGCTTCGAGCCGCCCTTTCTAGCTT  
CCTGGCCGGCTCTAGAACAATTCAGGCTTCGCTGCGACTAGACCTCAGCTCCAACATATGCA  
TTCTGAAGAAAGATGGCTGAGATGACAGAATGCTTTATTTTGGAAGAAACAATGTTCTAGG  
TCAAACCTGAGTCTACCAAATGCAGACTTTCACAATGGTTCTAGAAGAAATCTGGACAAGTCT  
TTTCATGTGGTTTTTCTACGCATTGATTCCATGTTTGCTCACAGATGAAGTGGCCATTCTGC  
CTGCCCCCTCAGAACCTCTCTGTACTCTCAACCAACATGAAGCATCTCTTGATGTGGAGCCCA  
GTGATCGCGCCTGGAGAAACAGTGTACTATTCTGTCTGAATACCAGGGGGAGTACGAGAGCCT  
GTACACGAGCCACATCTGGATCCCCAGCAGCTGGTGCTCACTCACTGAAGGTCCTGAGTGTG  
ATGTCACTGATGACATCACGGCCACTGTGCCATACAACCTTTGTGTCAGGGGCCACATTGGGC  
TCACAGACCTCAGCCTGGAGCATCCTGAAGCATCCCTTTAATAGAACTCAACCATCCTTAC  
CCGACCTGGGATGGAGATCACCAAAGATGGCTTNCACCTGGTTATTGAGCTGGAGGACCTGG  
GGCCCCAGTTTGAGTTCCTTGTGGCCTANTGGAGGAGGGGCGAACCCCTTGCGGCGCAAGGG  
GTTNGCGAACCCCTTGCGGCCGCTGGGGTATCTCTCGAGAAAAGAGAGGCCCAATATGACCCAC  
ATACTCAATATGGACGAANTGCTATTGTCCACCTGTTTGAGTGGCGCTGGGTGAT

119/330

**FIGURE 119**

CGGACGCGTGGGCCGCCACCTCCGGAACAAGCC**ATG**GTGGCGGCGACGGTGGCAGCGGCGTG  
GCTGCTCCTGTGGGCTGCGGCCTGCGCGCAGCAGGAGCAGGACTTCTACGACTTCAAGGCGG  
TCAACATCCGGGGCAAACCTGGTGTCGCTGGAGAAGTACCGCGGATCGGTGTCCCTGGTGGTG  
AATGTGGCCAGCGAGTGCGGCTTACAGACCAGCACTACCGAGCCCTGCAGCAGCTGCAGCG  
AGACCTGGGCCCCCACCACCTTTAACGTGCTCGCCTTCCCCTGCAACCAGTTTGGCCAACAGG  
AGCCTGACAGCAACAAGGAGATTGAGAGCTTTGCCCCGCCGCACCTACAGTGTCTCATTCCCC  
ATGTTTAGCAAGATTGCAGTCACCGGTACTGGTGCCCATCCTGCCTTCAAGTACCTGGCCCA  
GACTTCTGGGAAGGAGCCCACCTGGAACCTTCTGGAAGTACCTAGTAGCCCCAGATGGAAAGG  
TGGTAGGGGCTTGGGACCCAACCTGTGTCAGTGGAGGAGGTCAGACCCCAGATCACAGCGCTC  
GTGAGGAAGCTCATCCTACTGAAGCGAGAAGACTT**TAA**CCACCGCGTCTCCTCCTCCACCA  
CCTCATCCCGCCCACCTGTGTGGGGCTGACCAATGCAAACCTCAAATGGTGCTTCAAAGGGAG  
AGACCCACTGACTCTCCTTCCTTTACTCTTATGCCATTGGTCCCATCATTCTTGTGGGGGAA  
AAATTCTAGTATTTTGATTATTTGAATCTTACAGCAACAAATAGGAACTCCTGGCCAATGAG  
AGCTCTTGACCAGTGAATCACCAGCCGATACGAACGTCTTGCCAACAAAAATGTGTGGCAAA  
TAGAAGTATATCAAGCAATAATCTCCCACCCAAGGCTTCTGTAAACTGGGACCAATGATTAC  
CTCATAGGGCTGTTGTGAGGATTAGGATGAAATACCTGTGAAAGTGCCTAGGCAGTGCCAGC  
CAAATAGGAGGCATTCAATGAACATTTTTTGCATATAAACCAAAAAATACTTGTTATCAAT  
AAAAACTTGCATCCAACATGAATTTCCAGCCGATGATAATCCAGGCCAAAGGTTTAGTTGTT  
GTTATTTCTCTGTATTATTTTCTTCATTACAAAAGAAATGCAAGTTCATTGTAACAATCCA  
AACAAATACCTCACGATATAAAATAAAAAATGAAAGTATCCTCCTCAAAAA

120/330

**FIGURE 120**

MVAATVAAAWLLLWAAACAQQEQDFYDFKAVNIRGKLVSLVKYRGSVSLVVNVASECGFTDQ  
HYRALQQQLQRDLGPHHFNVLAFFPCNQFGQQEPDSNKEIESFARRTYSVSFFPMFSKIAVTGTG  
AHPAFKYLAQTSKGKEPTWNFWKYLVA PDGKVVGAWDPTVSVEEVRPQITALVRKLILLKREDL

121/330

**FIGURE 121**

CGGACGCGTGGGCGGGCCGGGACGCAGGGCAAAGCGAGCCATGGCTGTCTACGTCGGGATGC  
TGCGCCTGGGGAGGCTGTGCGCCGGGAGCTCGGGGGTGTGGGGGCCCGGGCCGCCCTCTCT  
CGGAGTTGGCAGGAAGCCAGGTTGCAGGGTGTCCGCTTCCTCAGTTCCAGAGAGGTGGATCG  
CATGGTCTCCACGCCCATCGGAGGCCCTCAGCTACGTTGAGGGGTGCACCAAAAAGCATCTTA  
ACAGCAAGACTGTGGGCCAGTGCCTGGAGACCACAGCACAGAGGGTCCCAGAACGAGAGGCC  
TTGGTCGTCCTCCATGAAGACGTCAGGTTGACCTTTGCCCAACTCAAGGAGGAGGTGGACAA  
AGCTGCTTCTGGCCTCCTGAGCATTGGCCTCTGCAAAGGTGACCGGCTGGGCATGTGGGGAC  
CTAACTCCTATGCATGGGTGCTCATGCAGTTGGCCACCGCCCAGGCGGGCATCATTCTGGTG  
TCTGTGAACCCAGCCTACCAGGCTATGGAAGTGGAGTATGTCCTCAAGAAGGTGGGCTGCAA  
GGCCCTTGTGTTCCCCAAGCAATTCAAGACCCAGCAATACTACAACGTCTGAAGCAGATCT  
GTCCAGAAGTGGAGAATGCCCAGCCAGGGGCCCTTGAAGAGTCAGAGGCTCCCAGATCTGACC  
ACAGTCATCTCGGTGGATGCCCCCTTGGCGGGGACCCTGCTCCTGGATGAAGTGGTGGCGGC  
TGGCAGCACACGGCAGCATCTGGACCAGCTCCAATACAACCAGCAGTTCCTGTCTGCCATG  
ACCCCATCAACATCCAGTTACCTCGGGGACAACAGGCAGCCCCAAGGGGGGCCACCCTCTCC  
CACTACAACATTGTCAACAACCTCCAACATTTTAGGAGAGCGCCTGAAACTGCATGAGAAGAC  
ACCAGAGCAGTTGCGGATGATCCTGCCCCAACCCCTGTACCATTGCCTGGGTTCCTGGCAG  
GCACAATGATGTGTCTGATGTACGGTGCCACCCTCATCCTGGCCTCTCCCATCTTCAATGGC  
AAGAAGGCACTGGAGGCCATCAGCAGAGAGAGAGGCACCTTCCTGTATGGTACCCCCACGAT  
GTTCTGTGGACATTCTGAACCAGCCAGACTTCTCCAGTTATGACATCTCGACCATGTGTGGAG  
GTGTCAATTGCTGGGTCCCCTGCACCTCCAGAGTTGATCCGAGCCATCATCAACAAGATAAAT  
ATGAAGGACCTGGTGGTTGCTTATGGAACCACAGAGAACAGTCCCGTGACATTCGCGCACTT  
CCCTGAGGACACTGTGGAGCAGAAGGCAGAAAGCGTGGGCAGAATTATGCCTCACACGGAGG  
CCCGGATCATGAACATGGAGGCAGGGACGCTGGCAAAGCTGAACACGCCCGGGGAGCTGTGC  
ATCCGAGGGTACTGCGTCATGCTGGGCTACTGGGGTGAGCCTCAGAAGACAGAGGAAGCAGT  
GGATCAGGACAAGTGGTATTGGACAGGAGATGTCGCCACAATGAATGAGCAGGGCTTCTGCA  
AGATCGTGGGCCGCTCTAAGGATATGATCATCCGGGGTGGTGAGAACATCTACCCCGCAGAG  
CTCGAGGACTTCTTTACACACACCCGAAGGTGCAGGAAGTGCAGGTGGTGGGAGTGAAGGA  
CGATCGGATGGGGGAAGAGATTTGTGCCTGCATTGCGCTGAAGGACGGGGAGGAGACCACGG  
TGGAGGAGATAAAAGCTTTCTGCAAAGGGAAGATCTCTCACTTCAAGATTCCGAAGTACATC  
GTGTTTGTCAAACTACCCCTCACCATTTAGGAAAGATCCAGAAATTCAAACCTCGAGA  
GCAGATGGAACGACATCTAAATCTGTGAATAAAGCAGCAGGCCTGTCCTGGCCGGTTGGCTT  
GACTCTCTCCTGTCAGAATGCAACCTGGCTTTATGCACCTAGATGTCCCCAGCACCCAGTTC  
TGAGCCAGGCACATCAAATGTCAAGGAATTGACTGAACGAACTAAGAGCTCCTGGATGGGTC  
CGGGAACCTCGCCTGGGCACAAGGTGCCAAAAGGCAGGCAGCCTGCCAGGCCCTCCCTCCTG  
TCCATCCCCACATTCCCCTGTCTGTCTTGTGATTTGGCATAAAGAGCTTCTGTTTTCTTT  
GAAAAAAAAAAAAAAAAA

122/330

**FIGURE 122**

MAVYVGMLRLGRLCAGSSGVLGARAALSRSWQEARLQGVRFLLSSREVDRMVSTPIGGLSYVQ  
GCTKKHLNSKTVGQCLETTAQRVPEREALVVLHEDVRLTFAQLKEEVDKAASGLLSIGLCKG  
DRLGMWGPNSYAWVLMQLATAQAGIILVSVNPAYQAMELEYVLKKVGCKALVFPKQFKTQQY  
YNVLKQICPEVENAQPGALKSQRLPDLTTVISVDAPLPGTLLLDEVVAAGSTRQHLDQLQYN  
QQFLSCHDPINIQFTSGTTGSPKGATLSHYNIVNNSNILGERLKLHEKTPEQLRMILPNPLY  
HCLGSVAGTMMCLMYGATLILASPIFNGKKALEAISRRERGTFLYGTPTMFVDILNQPDFSSY  
DISTMCGGVIAGSPAPPELIRAIINKINMKDLVVAYGTTENSPVTFAHFPEDTVEQKAESVG  
RIMPHTEARIMNMEAGTLAKLNTPGELCIRGYCVMLGYWGEPQKTEEAVDQDKWYWTGDVAT  
MNEQGFCCKIVGRSKDMIIRGGENIYPAELEDDFFHTHPKVQEVQVVGKDDRMGEEICACIRL  
KDGEETTVEEIKAFCKGKISHFKIPKYIVFVTNYPLTISGKIQKFKLREQMERHLNL

**Signal Peptide:**

amino acids 1-22

**Transmembrane Domains:**

amino acids 140-161, 213-229, 312-334

**Putative AMP-binding Domain Signature:**

amino acids 260-271

**N-myristoylation Sites:**amino acids 19-24, 22-27, 120-125, 203-208, 268-273, 272-277,  
314-319, 318-323, 379-384, 380-385, 409-413**N-glycosylation Site:**

amino acids 282-285

123/330

**FIGURE 123**

CAACTCCAACATTTTAGGAGAGCGCCTGAAACTGCATGAGAAGACACCAGAGCAGTTGCGGA  
TGATCCTGCCCCAACCCCCTGTACCATTCGCTGGGTTCCGTGGCAGGCACAATGATGTGTCTG  
ATGTACGGTGCCACCCTCATCCTGGCCTCTCCCATCTTCAATGGCAAGAAGGCACTGGAGGC  
CATCAGCAGAGAGAGAGAGGCACCTTCCTGTATGGTACCCCCACGATGTTTCGTGGACATTCTGA  
ACCAGCCAGACTTCTCCAGTTATGACATCTCGACCATGTGTGGAGGTGTCATTGCTGGGTCC  
CCTGCACCTCCAGAGTTGATCCGAGCCATCATCAACAAGATAAATATGAAGGACCTGGTGGT  
TGCTTATGGAACCACAGAGAACAGTCCCGTGACATTCGCGCACTTCCCTGAGGACACTGTGG  
AGCAGAAGGCAGAAAGCGTGGGCAGAATTATGCCTCACACGGAGGCGCGGATCATGAACATG  
GAGGCAGGGACGCTGGCAAAGCTGAACACGCCCCGGGGAGCTGTGCATCCGAGGGTACTGCGT  
CATGCTGGGCTACTGGGGTGAGCCTCAGAAGACAGAGGAAGCAGTGGATCAGGACAAGTGGT  
ATTGGACAGGAGATGTCGCCAC



124/330

**FIGURE 124**

GAGCAGGACGGAGCC**ATG**GACCCCGCCAGGAAAGCAGGTGCCCAGGCCATGATCTGGACTGC  
AGGCTGGCTGCTGCTGCTGCTGCTTCGCGGAGGAGCGCAGGCCCTGGAGTGCTACAGCTGCG  
TGCAGAAAGCAGATGACGGATGCTCCCCGAACAAGATGAAGACAGTGAAGTGCGCGCCGGGC  
GTGGACGTCTGCACCGAGGCCGTGGGGGCGGTGGAGACCATCCACGGACAATTCTCGCTGGC  
AGTGCGGGGTTGCGGTTTCGGGACTCCCCGGCAAGAATGACCGCGGCCTGGATCTTCACGGGC  
TTCTGGCGTTCATCCAGCTGCAGCAATGCGCTCAGGATCGCTGCAACGCCAAGCTCAACCTC  
ACCTCGCGGGCGCTCGACCCGGCAGGTAATGAGAGTGATACCCGCCCAACGGCGTGGAGTG  
CTACAGCTGTGTGGGCCTGAGCCGGGAGGCGTGCCAGGGTACATCGCCGCCGGTCTGTGAGCT  
GCTACAACGCCAGCGATCATGTCTACAAGGGCTGCTTCGACGGCAACGTCACCTTGACGGCA  
GCTAATGTGACTGTGTCCTTGCTGTCCGGGGCTGTGTCCAGGATGAATTCTGCACTCGGGA  
TGGAGTAACAGGCCCAGGGTTACGCTCAGTGGCTCCTGTTGCCAGGGGTCCCCTGTAACT  
CTGACCTCCGCAACAAGACCTACTTCTCCCCTCGAATCCCACCCCTTGTCCGGCTGCCCCCT  
CCAGAGCCCACGACTGTGGCCTCAACCACATCTGTCAACACTTCTACCTCGGCCCCAGTGAG  
ACCCACATCCACCACCAAACCCATGCCAGCGCCAACCAGTCAGACTCCGAGACAGGGAGTAG  
AACACGAGGCCTCCCGGGATGAGGAGCCCAGGTTGACTGGAGGCGCCGCTGGCCACCAGGAC  
CGCAGCAATTCAGGGCAGTATCCTGCAAAAGGGGGGCCCCAGCAGCCCCATAATAAAGGCTG  
TGTGGCTCCCACAGCTGGATTGGCAGCCCTTCTGTTGGCCGTGGCTGCTGGTGTCTACTGT**I**  
**GA**GCTTCTCCACCTGGAAATTTCCCTCTCACCTACTTCTCTGGCCCTGGGTACCCCTCTTCT  
CATCACTTCCTGTTCCCACTGACTGGGCTGGCCAGCCCCTGTTTTTCCAACATTCCC  
CAGTATCCCCAGCTTCTGCTGCGCTGGTTTTCGGCTTTGGGAAATAAAATACCGTTGTATAT  
ATTCTGCCAGGGGTGTTCTAGCTTTTTGAGGACAGCTCCTGTATCCTTCTCATCCTTGTCTC  
TCCGCTTGTCTCTTGTGATGTTAGGACAGAGTGAGAGAAGTCAGCTGTCACGGGGAAGGTG  
AGAGAGAGGATGCTAAGCTTCCTACTCACTTCTCCTAGCCAGCCTGGACTTTGGAGCGTGG  
GGTGGGTGGGACAATGGCTCCCCACTCTAAGCACTGCCTCCCCTACTCCCCGCATCTTTGGG  
GAATCGGTTCCCCATATGTCTTCCTTACTAGACTGTGAGCTCCTCGAGGGGGGGCCCGGTAC  
CCAATTCGCCCTATAGTGAGTCGTA

125/330

**FIGURE 125**

MDPARKAGAQAMIWTAGWLLLLLLLRGGAQALECYSCVQKADDGCS PNKMKTVKCAPGVDVCT  
EAVGAVETIHGQFSLAVRGCGSGLPGKNDRGLDLHGLLAFIQLQOCAQDRCNAKLNLT SRAL  
DPAGNESAYPPNGVECYSCVGLSREACQGTSPPVVSCYNASDHVYKGC FDGNVTLTAAANVTV  
SLPVRGCVQDEFCTR DGVTGPGFTLSGSCCQGSRCNSDLRNKTYFSPRI PPLVRLPPPEPTT  
VASTTSVTTST SAPVRPTSTTKPMPAPTSQTPRQGEHEASRDEEPRLTGGAAGHQDRSNSG  
QYPAKGGPQQPHNKGCVAPTAGLAALLLAVAAGVLL

126/330

**FIGURE 126**

[illegible]

127/330

**FIGURE 127**

MELVLVFLCSLLAPMVLASAAEKEKEMDPFHYDYQTLRIGGLVFAVVLFSVGILLILSRCK  
CSFNQKPRAPGDEEAQVENLITANATEPQKQRTEVQPSGGSLWNLRRLLLEPLDANVDA

128/330

**FIGURE 128**

AAACTTGACGCC**ATG**AAGATCCCGGTCCTTCCTGCCGTGGTGCTCCTCTCCCTCCTGGTGCT  
CCACTCTGCCCAGGGAGCCACCCTGGGTGGTCCTGAGGAAGAAAGCACCATTGAGAATTATG  
CGTCACGACCCGAGGCCTTTAACACCCCGTTCCTGAACATCGACAAATTGCGATCTGCGTTT  
AAGGCTGATGAGTTCCTGAACTGGCACGCCCTCTTTGAGTCTATCAAAAGGAACTTCCTTT  
CCTCAACTGGGATGCCTTTCCTAAGCTGAAAGGACTGAGGAGCGCAACTCCTGATGCCCAG**T**  
**G**ACCATGACCTCCACTGGAAGAGGGGGCTAGCGTGAGCGCTGATTCTCAACCTACCATAACT  
CTTTCCTGCCTCAGGAACTCCAATAAAACATTTTCCATCCAAA

129/330

**FIGURE 129**

MKIPVLPVAVLLSLLVLHSAQGATLGGPEEESTIENYASRPEAFNTPFLNIDKLRSFAKDE  
FLNWHALFESIKRKLPFLNWDAFPKLGKGLRSATPDAQ

130/330

**FIGURE 130**

CAGTTCTGAAATCAATGGAGTTAATTTAGGGAATACAAACCAGCC**ATG**GGGGTGGAGATTGC  
CTTTGCCTCAGTGATTCTCACCTGCCTCTCCCTTCTGGCAGCAGGAGTCTCCCAGGTTGTTC  
TTCTCCAGCCAGTTCCAACCTCAGGAGACAGGTCCCAAGGCCATGGGAGATCTCTCCTGTGGC  
TTTGCCGGCCACTCA**TGA**GAGTGTTTTTGTGTAAAGTATTTTTTTAGAATACTGTTGACTTCT  
TCATGATTTAATAACCATCCTTTGCGAAGTTTTATGAGGCTTTAGGGGAATGTCAACCCTCA  
AATTTTTGTTATACTAGATGGCTTCCATTTACCCACCACTATTTTAAGGTCCCTTTATTTTT  
AGGTTCAAGGTTCAATTTGACTTGAGAAAGTGCCCTTCTGCAGCTTCATTGATTTTGTTTATC  
TTCATATTAATTGTAACGATTAAAAAGAATAAGAGCACGCAGACCTCTAGGAGAATATTT  
TATCCCTGGGTGCCCCTGACACATTTATGTAGTGATCCCACAAATGTGATTGTTAATTTAAA  
TGTTATTCTAATATTAGTACATTCAGTTGTGATGTAATATGAATAACCAGAATCTATTTCTT  
AAAAGTTTTGAGTATATTTTTCAACTAGATATTTGTATAGAAAGACTGAATAGTGATG

131/330

**FIGURE 131**

MGVEIAFASVILTCLSLAAGVSQVLLQPVPTQETGPKAMGDLSCGFAGHS



132/330

**FIGURE 132**

GGGGAATCTGCAGTAGGTCTGCCGGCG**ATG**GAGTGGTGGGCTAGCTCGCCGCTTCGGCTCTG  
GCTGCTGTTGTTCCCTCCTGCCCTCAGCGCAGGGCCGCCAGAAGGAGTCAGGTTCAAAATGGA  
AAGTATTTATTGACCAAATTAACAGGTCTTTGGAGAATTACGAACCATGTTCAAGTCAAAC  
TGCAGCTGCTACCATGGTGTCTAGAGAAGAGGATCTAACTCCTTTCCGAGGAGGCATCTCCAG  
GAAGATGATGGCAGAGGTAGTCAGACGGAAGCTAGGGACCCACTATCAGATCACTAAGAACA  
GACTGTACCGGGAAAATGACTGCATGTTCCCCTCAAGGTGTAGTGGTGTGAGCACTTTATT  
TTGGAAGTGATCGGGCGTCTCCCTGACATGGAGATGGTGATCAATGTACGAGATTATCCTCA  
GGTTCCTAAATGGATGGAGCCTGCCATCCCAGTCTTCTCCTTCAGTAAGACATCAGAGTACC  
ATGATATCATGTATCCTGCTTGGACATTTTGGGAAGGGGGACCTGCTGTTTGGCCAATTTAT  
CCTACAGGTCTTGGACGGTGGGACCTCTTCAGAGAAGATCTGGTAAGGTCAGCAGCACAGTG  
GCCATGGAAAAAGAAAACTCTACAGCATATTTCCGAGGATCAAGGACAAGTCCAGAACGAG  
ATCCTCTCATTCTTCTGTCTCGGAAAAACCCAAAACCTTGTGATGCAGAATACACCAAAAAC  
CAGGCCTGGAAATCTATGAAAGATACCTTAGGAAAGCCAGCTGCTAAGGATGTCCATCTTGT  
GGATCACTGCAAATACAAGTATCTGTTTAATTTTCGAGGCGTAGCTGCAAGTTTCCGGTTTA  
AACACCTCTTCCTGTGTGGCTCACTTGTTTTCCATGTTGGTGATGAGTGGCTAGAATTCTTC  
TATCCACAGCTGAAGCCATGGGTTCATATATCCCAGTCAAAACAGATCTCTCCAATGTCCA  
AGAGCTGTTACAATTTGTAAAAGCAAATGATGATGTAGCTCAAGAGATTGCTGAAAGGGGAA  
GCCAGTTTATTAGGAACCATTTGCAGATGGATGACATCACCTGTTACTGGGAGAACCTCTTG  
AGTGAATACTCTAAATTCCTGTCTTATAATGTAACGAGAAGGAAAGGTTATGATCAAATTAT  
TCCCAAAATGTTGAAAACCTGAACTA**TAG**TAGTCATCATAGGACCATAGTCCTCTTTGTGGCA  
ACAGATCTCAGATATCCTACGGTGAGAAGCTTACCATAAGCTTGGCTCCTATACCTTGAATA  
TCTGCTATCAAGCCAAATACCTGGTTTTCTTATCATGCTGCACCCAGAGCAACTCTTGAGA  
AAGATTTAAAATGTGTCTAATACACTGATATGAAGCAGTTCAACTTTTTGGATGAATAAGGA  
CCAGAAATCGTGAGATGTGGATTTTGAACCCAACTCTACCTTTTCATTTTCTTAAGACCAATC  
ACAGCTTGTGCCTCAGATCATCCACCTGTGTGAGTCCATCACTGTGAAATTGACTGTGTCCA  
TGTGATGATGCCCTTTGTCCCATTATTTGGAGCAGAAAATTCGTCATTTGGAAGTAGTACAA  
CTCATTGCTGGAATTGTGAAATTATTCAAGGCGTGATCTCTGTCACTTTATTTTAATGTAGG  
AAACCTATGGGGTTTATGAAAAATACTTGGGGATCATTCTCTGAATGGTCTAAGGAAGCGG  
TAGCCATGCCATGCAATGATGTAGGAGTTCTCTTTTGTAAAACCATAAACTCTGTTACTCAG  
GAGGTTTCTATAATGCCACATAGAAAGAGGCCAATTGCATGAGTAATTATTGCAATTGGATT  
TCAGGTTCCCTTTTTGTGCCTTCATGCCCTACTTCTTAATGCCTCTCTAAAGCCAAA

133/330

**FIGURE 133**

MEWWASSPLRLWLLLFLLPQAQGRQKESGSKWKVFIDQINRSLENYEPCSSQNCSCYHGVIE  
EDLTPFRGGISRKMAEVVRRKLGTHYQITKNRLYREND CMFPSRCSGVEHFILEVIGRLPD  
MEMVINVRDYPQVPKWMEPAIPVFSFSKTSEYHDIMYPAWTFWEGGPAVWPIYPTGLGRWDL  
FREDLVRSAQWPWKKNSTAYFRGSRTSPERDPLILLSRKKNPKLVDAEYTKNQAWKSMKDT  
LGKPAAKDVHLVDHCKYKYLNFNFRGVAASF RFKHLFLCGSLVFHVGDEWLEFFYPQLKPWVH  
YIPVKTDL SNVQELLQFVKANDDVAQEIAERGSQFIRNHLQMD DITCYWENLLSEYSKFLSY  
NVTRRKGYDQII PKMLKTEL

134/330

**FIGURE 134**

CACCCCTCCATTTCTCGCC**ATG**GGCCCTGCACTGCTCCTGATCCCTGCTGCCCTCGCCTCTT  
TCATCCTGGCCTTTGGCACCGGAGTGGAGTTCGTGCGCTTTACCTCCCTTCGGCCACTTCTT  
GGAGGGATCCCGGAGTCTGGTGGTCCGGATGCCCCGCCAGGGATGGCTGGCTGCCCTGCAGGA  
CCGCAGCATCCTTGCCCCCTGGCATGGGATCTGGGGCTCCTGCTTCTATTTGTTGGGCAGC  
ACAGCCTCATGGCAGCTGAAAGAGTGAAGGCATGGACATCCCGGTACTTTGGGGTCCTTCAG  
AGGTCACTGTATGTGGCCTGCACTGCCCTGGCCTTGCAGCTGGTGATGCGGTACTGGGAGCC  
CATACCCAAAGGCCCTGTGTTGTGGGAGGCTCGGGCTGAGCCATGGGCCACCTGGGTGCCGC  
TCCTCTGCTTTGTGCTCCATGTCATCTCCTGGCTCCTCATCTTTAGCATCCTTCTCGTCTTT  
GACTATGCTGAGCTCATGGGCCTCAAACAGGTATACTACCATGTGCTGGGGCTGGGCGAGCC  
TCTGGCCCTGAAGTCTCCCCGGGCTCTCAGACTCTTCTCCACCTGCGCCACCCAGTGTGTG  
TGGAGCTGCTGACAGTGCTGTGGGTGGTGCCTACCCTGGGCACGGACCGTCTCCTCCTTGCT  
TTCCTCCTTACCCTCTACCTGGGCCTGGCTCACGGGCTTGATCAGCAAGACCTCCGCTACCT  
CCGGGCCCAGCTACAAAGAAAACCTCCACCTGCTCTCTCGGCCCCAGGATGGGGAGGCAGAGT**G**  
**A**GGAGCTCACTCTGGTTACAAGCCCTGTTCTTCTCCTCTCCCACTGAATTCTAAATCCTTAAC  
ATCCAGGCCCTGGCTGCTTCATGCCAGAGGCCCAAATCCATGGACTGAAGGAGATGCCCTT  
CTACTACTTGAGACTTTATTCTCTGGGTCCAGCTCCATACCCTAAATTCTGAGTTTCAGCCA  
CTGAACTCCAAGGTCCACTTCTCACCAGCAAGGAAGAGTGGGGTATGGAAGTCATCTGTCCC  
TTCAGTGTTTAGAGCATGACACTCTCCCCCTCAACAGCCTCCTGAGAAGGAAAGGATCTGCC  
CTGACCACTCCCCCTGGCACTGTTACTTGCCTCTGCGCCTCAGGGGTCCCCTTCTGCACCGCT  
GGCTTCCACTCCAAGAAGGTGGACCAGGGTCTGCAAGTTCAACGGTCATAGCTGTCCCTCCA  
GGCCCCAACCTTGCCTCACCCTCCCGGCCCTAGTCTCTGCACCTCCTTAGGCCCTGCCTCT  
GGGCTCAGACCCCAACCTAGTCAAGGGGATTCTCCTGCTCTTAACTCGATGACTTGGGGCTC  
CCTGCTCTCCCGAGGAAGATGCTCTGCAGGAAAATAAAAGTCAGCCTTTTTCTAAAAAAA

135/330

**FIGURE 135**

MAPALLLI PAALASFILAFGTGVEFVRFTSLRPLLGGIPESGGPDARQGWLAALQDRSILAP  
LAWDLGLLLLFVVGQHSMAAERVKAWTSRYFGVLQRSLYVACTALALQLVMRYWEPI PKGPV  
LWEARAEPWATWVPLLCFVLHVISWLLIFSILLVFDYAELMGLKQVYYHVLGLGEPLALKSP  
RALRLFSHLRHPVCVELLTVLWVPTLGTDRLLLAFLLTLYLGLAHGLDQQDLRYLRAQLQR  
KLHLLSRPQDGEAE

**Signal sequence:**

amino acids 1-13

**Transmembrane domains:**

amino acids 58-76, 99-113, 141-159, 203-222

**N-myristoylation sites:**

amino acids 37-43, 42-48, 229-235

136/330

**FIGURE 136**

CCGAGCACAGGAGATTGCCTGCGTTT TAGGAGGTGGCTGCGTTGTGGGAAAAGCTATCAAGGA  
AGAAATTGCCAAACCATGTCTTTTTTTCTGTTTTTCAGAGTAGTTCACAACAGATCTGAGTGT  
TTTAATTAAGCATGGAATACAGAAAACAACAAAAA ACTTAAGCTTTAATTTTCATCTGGAATT  
CCACAGTTTTCTTAGCTCCCTGGACCCGGTTGACCTGTTGGCTCTTCCCGCTGGCTGCTCTA  
TCACGTGGTGCTCTCCGACTACTCACCCCGAGTGTAAGAACCTTCGGCTCGCGTGCTTCTG  
AGCTGCTGTGGATGGCCTCGGCTCTCTGGACTGTCCTTCCGAGTAGGATGTCACTGAGATCC  
CTCAAATGGAGCCTCCTGCTGCTGTCACTCCTGAGTTTTCTTTGTGATGTGGTACCTCAGCCT  
TCCCCACTACAATGTGATAGAACGCGTGA ACTGGATGTACTTCTATGAGTATGAGCCGATTT  
ACAGACAAGACTTTCACTTCACACTTCGAGAGCATTCAAACTGCTCTCATCAAAATCCATTT  
CTGGTCATTCTGGTGACCTCCCACCCTTCAGATGTGAAAGCCAGGCAGGCCATTAGAGTTAC  
TTGGGGTGAAAAAAAGTCTTGGTGGGGATATGAGGTTCTTACATTTTTCTTATTAGGCCAAG  
AGGCTGAAAAGGAAGACAAAATGTTGGCATTGTCCTTAGAGGATGAACACCTTCTTTATGGT  
GACATAATCCGACAAGATTTTTTTAGACACATATAATAACCTGACCTTGAAAACCATTTATGGC  
ATTCAGGTGGGTAACTGAGTTTTGCCCCAATGCCAAGTACGTAATGAAGACAGACACTGATG  
TTTTTCATCAATACTGGCAATTTAGTGAAGTATCTTTTAAACCTAAACCACTCAGAGAAGTTT  
TTCACAGGTTATCCTCTAATTGATAATTATTCCTATAGAGGATTTTACCAAAAAACCCATAT  
TTCTTACCAGGAGTATCCTTTCAAGGTGTTCCCTCCATACTGCAGTGGGTTGGGTTATATAA  
TGTCCAGAGATTTGGTGCCAAGGATCTATGAAATGATGGGTACGTAAAACCCATCAAGTTT  
GAAGATGTTTATGTGCGGATCTGTTTGAATTTATTTAAAGTGAACATTCATATTCCAGAAGA  
CACAAATCTTTTCTTTCTATATAGAATCCATTTGGATGTCTGTCAACTGAGACGTGTGATTG  
CAGCCCATGGCTTTTCTTCCAAGGAGATCATCACTTTTTTGGCAGGTCATGCTAAGGAACACC  
ACATGCCATTATTAACTTCACATTCTACAAAAAGCCTAGAAGGACAGGATACCTTGTGGAAA  
GTGTTAAATAAAGTAGGTACTGTGGAAAATTCATGGGGAGGTCAGTGTGCTGGCTTACACTG  
AACTGAAACTCATGAAAAACCCAGACTGGAGACTGGAGGGTTACACTTGTGATTTATTAGTC  
AGGCCCTTCAAAGATGATATGTGGAGGAATTAAATATAAAGGAATTGGAGGTTTTTGCTAAA  
GAAATTAATAGGACCAAACAATTTGGACATGTCATTCTGTAGACTAGAATTTCTTAAAAGGG  
TGTTACTGAGTTATAAGCTCACTAGGCTGTAAAAACAAAACAATGTAGAGTTTTATTATTG  
AACAAATGTAGTCACTTGAAGGTTTTGTGTATATCTTATGTGGATTACCAATTTAAAAATATA  
TGTAGTTCTGTGTCAAAAAACTTCTTCACTGAAGTTATACTGAACAAAATTTTACCTGTTTT  
TGGTCATTTATAAAGTACTTCAAGATGTTGCAGTATTTACAGTTATTATTATTTAAAATTA  
CTTCAACTTTGTGTTTTTTAAATGTTTTGACGATTTCAATACAAGATAAAAAGGATAGTGAAT  
CATTCTTTACATGCAAACATTTTCCAGTTACTTAACTGATCAGTTTATTATTGATACATCAC  
TCCATTAATGTAAAGTCATAGGTCATTATTGCATATCAGTAATCTCTTGGACTTTGTAAAT  
ATTTTACTGTGGTAATATAGAGAAGAATTAAAGCAAGAAAATCTGAAA

137/330

**FIGURE 137**

MASALWTVLPSRMSLRSLKWSLLLLSLLSFFVMWYLSLPHYNVIERVNWMYFYEYEPYRQD  
FHFTLREHSNCSHQNPFLVILVTSHPSDVKARQAIRVTWGEKKSWWGYEVLTFLLGQEA EK  
EDKMLALSLEDEHLLYGDIIRQDFLDTYNNLTTLKTIMAFRWVTEFCPNAKYVMKTDTDVFIN  
TGNLVKYLLNLNHSEKFFTGYPLIDNYSYRGFYQKTHISYQEYPFKVFPPYCSGLGYIMSRD  
LVPRIYEMMGHVKPIKFEDVYVGICLNLLKVNIHIPEDTNLFFLYRIHLDVCQLRRVIAAHG  
FSSKEIITFWQVMLRNTTCHY

138/330

**FIGURE 138**

CCTCTGTCCACTGCTTTTCGTGAAGACAAG**ATG**AAGTTCACAATTGTCTTTGCTGGACTTCTT  
GGAGTCTTTCTAGCTCCTGCCCTAGCTAACTATAATATCAACGTCAATGATGACAACAACAA  
TGCTGGAAGTGGGCAGCAGTCAGTGAGTGTCAACAATGAACACAATGTGGCCAATGTTGACA  
ATAACAACGGATGGGACTCCTGGAATTCCATCTGGGATTATGGAAATGGCTTTGCTGCAACC  
AGACTCTTTCAAAAGAAGACATGCATTGTGCACAAAATGAACAAGGAAGTCATGCCCTCCAT  
TCAATCCCTTGATGCACTGGTCAAGGAAAAGAAGCTTCAGGGTAAGGGACCAGGAGGACCAC  
CTCCCAAGGGCCTGATGTACTCAGTCAACCCAAACAAAGTCGATGACCTGAGCAAGTTCGGA  
AAAAACATTGCAAACATGTGTCGTGGGATTCCAACATACATGGCTGAGGAGATGCAAGAGGC  
AAGCCTGTTTTTTTTACTCAGGAACGTGCTACACGACCAGTGTACTATGGATTGTGGACATTT  
CCTTCTGTGGAGACACGGTGGAGAAC**TAA**ACAATTTTTTAAAGCCACTATGGATTTAGTCAT  
CTGAATATGCTGTGCAGAAAAAATATGGGCTCCAGTGGTTTTTTACCATGTCATTCTGAAATT  
TTTCTCTACTAGTTATGTTTGATTTCTTTAAGTTTCAATAAAATCATTTAGCATTGAAAAAAA

139/330

## **FIGURE 139**

MKFTIVFAGLLGVFLAPALANYNINVNDDNNNAGSGQQSVSVNNEHNVANVDNNNGWDSWNS  
IWDYGNGFAATRLFQKKTCIVHKMNKEVMPSIQSLDALVKEKKLQKGPGGPPPKGLMYSVN  
PNKVDDLKSKFGKNIANMCRGIPTYMAEEMQEASLFFYSGTCYTTSVLWIVDISFCGDTVEN

### **Signal Peptide:**

amino acids 1-20

### **N-myristoylation Sites:**

amino acids 67-72, 118-123, 163-168

### **Flavodoxin protein homology:**

amino acids 156-174



140/330

**FIGURE 140**

CATTTCTGAAACTAATCGTGTGAGAATTGACTTTGAAAAGCATTGCTTTTTTACAGAAGTATA  
TTAACTTTTTTAGGAGTAATTTCTAGTTTGGATTGTAATATGAAATAATTTAAAAGGGCTTCG  
CTCATATATAGGAAAATCGCATATGGTCCTAGTATTAAATTCTTATTGCTTACTGATTTTTT  
TGAGTTAAGAGTTGTTATATGCTAGAATATGAGGATGTGAATATAAATAAGAGAAGAAAAA  
GAATAAAGTAGATTGAGTCTCCAATTTTATGTAAGCTTCAGAAGAAGCTGGTTTGTTTACATG  
CAAGCTTATAGTTGAAATATTTTTTCAGGAATTAC**ATGA**ATGACAGTCTTCGAACCAATGTGT  
TTGTTTCGATTTCAACCAGAGACTATAGCATGTGCTTGCATCTACCTTGCAGCTAGAGCACTT  
CAGATTCGGTTGCCAACTCGTCCCCATTGGTTTCTTCTTTTTTGGTACTACAGAAGAGGAAAT  
CCAGGAAATCTGCATAGAAACACTTAGGCTTTATACCAGAAAAAAGCCAAACTATGAATTAC  
TGGAAAAAGAAGTAGAAAAAAGAAAAGTAGCCTTACAAGAAGCCAAATTTAAAAGCAAAGGGA  
TTGAATCCGGATGGAAGCTCCAGCCCTTTCAACCCTGGGTGGATTTTCTCCAGCCTCCAAGCC  
ATCATCACCAAGAGAAGTAAAAGCTGAAGAGAAATCACCAATCTCCATTAATGTGAAGACAG  
TCAAAAAAGAACCTGAGGATAGACAACAGGCTTCCAAAAGCCCTTACAATGGTGTAAAGAAA  
GACAGCAAGAGAAGTAGAAATAGCAGAAGTGCAAGTCGATCGAGGTCAAGAACACGATCACG  
TTCTAGATCACATACTCCAAGAAGACACTATAATAATAGGCGGAGTCGATCTGGAACATACA  
GCTCGAGATCAAGAAGCAGGTCCCGCAGTCACAGTGAAAGCCCTCGAAGACATCATAATCAT  
GGTTCTCCTCACCTTAAGGCCAAGCATAACCAGAGATGATTTAAAAGTTCAAACAGACATGG  
TCATAAAAGGAAAAAATCTCGTTCTCGATCTCAGAGCAAGTCTCGGGATCACTCAGATGCAG  
CCAAGAAACACAGGCATGAAAGGGGACATCATAGGGACAGGCGTGAACGATCTCGCTCCTTT  
GAGAGGTCCCATAAAAGCAAGCACCATGGTGGCAGTCGCTCAGGACATGGCAGGCACAGGCG  
**CTGA**CTTTCTCTTCCTTTGAGCCTGCATCAGTTCTTGGTTTTGCCTATCTACAGTGTGATGT  
ATGGACTCAATCAAAAACATTAAACGCAAACCTGATTAGGATTTGATTTCTTGAAACCCTCTA  
GGTCTCTAGAACACTGAGGACAGTTTCTTTTGAAAAGAACTATGTTAATTTTTTTGCACATT  
AAAATGCCCTAGCAGTATCTAATTTAAAACCATGGTCAGGTTCAATTGTACTTTATTATAGT  
TGTGTATTGTTTATTGCTATAAGAACTGGAGCGTGAATTCTGTAAAAATGTATCTTATTTTT  
ATACAGATAAAATTGCAGACACTGTTCTATTTAAGTGGTTATTTGTTTAAATGATGGTGAAT  
ACTTTCTTAACACTGGTTTGTCTGCATGTGTAAAGATTTTTTACAAGGAAATAAAATACAAAT  
CTTGTTTTTTCTAAAAAAAAAAAAAAAAAAGT

141/330

**FIGURE 141**

MNDSLRTNVFVRFQPETIACACIYLAARALQIPLPTRPHWFLLFGTTEEEIQEICIETLRLY  
TRKKPNYELLEKEVEKRRKVALQEAKLKAKGLNPDGTPALSTLGGFSPASKPSSPREVKAEEK  
SPISINVKTVKKEPEDRQQASKSPYNGVRKDSKRSRNSRSASRSRSRTRSRSRSHTPRRHYN  
NRRSRSGTYSSRSRSRSRSHSESPRRHHNHGSPHLKAKHTRDDLKSSNRHGHKRRKKSRSRSQ  
SKSRDHSDAAKKHRHERGHHRRDRRERSRSFERSHKSKHHGGSRSRGHGRHRR

142/330

**FIGURE 142**

TGGGGATAAAGGAAAAATGGTCAGGTATTAATGGCTTAAAGATTATTGGAAGGGGTTTATCA  
TTTTTTGAANNNTATTCGGGTCANAATTGNCTTTGAAAAGCATTGCTTTTTACAGAAATATAT  
TANCTTTTTAGAGTAATTTCTAGTTTGGATTGTAATATGAAATTATTTAAAAGGGCTTCGCT  
CATATATAGGAAAATCGCATATGGTCCTAGTATTAAATTNNTATTGCTTACTGATTTTTTTTG  
AGTTAAGAGTTGTTATATGNTAGAATATGAGGATGTGAATATAAATAAGAGAAGAAAAAAGA  
ATAAAGTAGATTGAGTCTCCAATTTTATGTAAGCTTCAGAAGAAGTGGTTTGTTTACATGCA  
AGCTTATAGTTGAAATATTTTTCAGGAATTACATGAATGACAGTCTTCGAACCAATGTGTTT  
GTTCGATTTCAACCAGAGANTATAGCATGTGCTTGCATCTACCTTGCAGNTAGAGCACTTCA  
GATTCCGTTGCCAACTNGTCCCCATTGGTTTCTTCTTTTGGTACTACAGAAGAGGAAATCC  
AGGAAATNTGCATAGAAACACTTAGGCTTTATACCAGAAAAAAGCCAACTATGAATTACTG  
GAAAAAGAAGTAGAAAAAAGAAAAGTAGCCTTACAAGAAGCCNAATTAAAAGCAAAGGGATT  
GAATCCGGATGGAAGTCCAGCCCTTCAACCCTGGGTGGATTTTCTCC

143/330

**FIGURE 143**

GGCACGAGGCCTCGTGCCAAGCTTGGCACGAGGGTGCACCGCGTTCTCGCACGCGTC**ATGGC**  
GGTCCTCGGAGTACAGCTGGTGGTGACCCTGCTCACTGCCACCCTCATGCACAGGCTGGCGC  
CACACTGCTCCTTCGCGCGCTGGCTGCTCTGTAAACGGCAGTTTGTTCGGATACAAGCACCCG  
TCTGAGGAGGAGCTTCGGGCCCTGGCGGGGAAGCCGAGGCCAGAGGCAGGAAAGAGCGGTG  
GGCCAATGGCCTTAGTGAGGAGAAGCCACTGTCTGTGCCCCGAGATGCCCCGTTCCAGCTGG  
AGACCTGCCCCCTCACGACCGTGGATGCCCTGGTCCTGCGCTTCTTCCTGGAGTACCAGTGG  
TTTGTGGACTTTGCTGTGTACTCGGGCGGCGTGTACCTCTTCACAGAGGCCTACTACTACAT  
GCTGGGACCAGCCAAGGAGACTAACATTGCTGTGTTCTGGTGCCTGCTCACGGTGACCTTCT  
CCATCAAGATGTTCCCTGACAGTGACACGGCTGTACTTCAGCGCCGAGGAGGGGGGTGAGCGC  
TCTGTCTGCCTCACCTTTGCCTTCCTCTTCCTGCTGCTGGCCATGCTGGTGCAAGTGGTGCG  
GGAGGAGACCCTCGAGCTGGGCCTGGAGCCTGGTCTGGCCAGCATGACCCAGAACTTAGAGC  
CACTTCTGAAGAAGCAGGGCTGGGACTGGGCGCTTCCTGTGGCCAAGCTGGCTATCCGCGTG  
GGACTGGCAGTGGTGGGCTCTGTGCTGGGTGCCTTCCTCACCTTCCCAGGCCTGCGGCTGGC  
CCAGACCCACCGGGACGCACTGACCATGTGCGAGGACAGACCCATGCTGCAGTTCTCCTGC  
ACACCAGCTTCCTGTCTCCCTGTTTCATCCTGTGGCTCTGGACAAAGCCCATTGCACGGGAC  
TTCCTGCACCAGCCGCCGTTTGGGGAGACGCGTTTCTCCCTGCTGTCCGATTCTGCCTTCGA  
CTCTGGGCGCCTCTGGTTGCTGGTGGTGTGCTGTGCCTGCTGCGGCTGGCGGTGACCCGGCCCC  
ACCTGCAGGCCTACCTGTGCCTGGCCAAGGCCCGGGTGGAGCAGCTGCGAAGGGAGGCTGGC  
CGCATCGAAGCCCGTGAAATCCAGCAGAGGGTGGTCCGAGTCTACTGCTATGTGACCGTGGT  
GAGCTTGCAGTACCTGACGCCGCTCATCCTCACCTCAACTGCACACTTCTGCTCAAGACGC  
TGGGAGGCTATTCTTGGGGCCTGGGCCAGCTCCTCTACTATCCCCCGACCCATCCTCAGCC  
AGCGCTGCCCCCATCGGCTCTGGGGAGGACGAAGTCCAGCAGACTGCAGCGCGGATTGCCGG  
GGCCCTGGGTGGCCTGCTTACTCCCCTCTTCCTCCGTGGCGTCTGGCCTACCTCATCTGGT  
GGACGGCTGCCTGCCAGCTGCTCGCCAGCCTTTTCGGCCTCTACTTCCACCAGCACTTGGCA  
GGCTCC**TAG**CTGCCTGCAGACCCTCCTGGGGCCCTGAGGTCTGTTCTGGGGCAGCGGGACA  
CTAGCCTGCCCCCTCTGTTTGCGCCCCCGTGTCCCCAGCTGCAAGGTGGGGCCGGACTCCCC  
GGCGTTCCTTACACACAGTGCCTGACCCGCGGCCCCCCTGGACGCCGAGTTTCTGCCTCA  
GAACTGTCTCTCCTGGGCCCAGCAGCATGAGGGTCCCGAGGCCATTGTCTCCGAAGCGTATG  
TGCCAGGTTTGAGTGGCGAGGGTGATGCTGGCTGCTCTTCTGAACAAATAAAGGAGCATGCC  
GATTTTAA

144/330

**FIGURE 144**

MAVLGVQLVVTLLTATLMHRLAPHCSFARWLLCNGSLFRYKHPSEEELRALAGKPRPRGRKE  
RWANGLSEEKPLSVPRDAPFQLETCPLTTVDALVLRFFLEYQWFVDFAVYSGGVYLFTEAYY  
YMLGPAKETNIAVFWCLLTVTFSIKMFLTVTRLYFSAEEGGERSVCLTFAFLFLLLAMLVQV  
VREETLELGLEPGLASMTQNLEPLLKKQGWDWALPVAKLAI RVGLAVVGSVLGAFLTFFGLR  
LAQTHRDALTMSEDRPMLQFLLHTSFLSPLFILWLWTKPIARDFLHQPPFGETRFSLLSDSA  
FDSGRLWLLVVLCLLRLAVTRPHLQAYLCLAKARVEQLRREAGRIEAREIQQRVVRVYCYVT  
VVS LQYLTPLILTLNCTLLLKTLGGYSWGLGPAPLLSPDPSSASAAPIGSGEDEVQOTAARI  
AGALGGLLTPLFLRGVLAYLIWWTAA CQLLASLFGLYFHQHLA GS

145/330

**FIGURE 145**

CGTTNGCACGCGTCAATGGCGGTCCTCGGAGTACAGCTGGTGGTGACCCTGCTCACTGCCAC  
CCTCATGCACAGGCTGGCGCCACACTGCTCCTTCGCGCGCTGGCTGCTCTGTAAACGGCAGTT  
TGTTCCGATACAAGCACCCGTNTTGAGGAGGAGCTTCGGGCCCTGGCGGGGAAGCCGAGGCC  
CAGAGGCAGGAAAGAGCGGTGGGCCAATGGCCTTAGTGAGGAGAAGCCACTGTCTGTGCCCC  
GAGATGCCCCGTTCCAGCTGGAGACCTGCCCCCTCACGACCGTGGATGCCCTGGTCCTGCGC  
TTCTTCCTGGAGTACCAGTGGTTTGTGGACTTTGCTGTGTACTCGGGCGGCGTGTACCTCTT  
CACAGAGGCCTACTACTACATGCTGGGACCAGCCAAGGAGACTAACATTGCTGTGTTCTGGT  
GCCTGCTCACAGTGACCTTCTCCATCAAGATGTTCTGACAGTGACACGGCTGTACTTCAGC  
GCCGAGGAGGGGGGTGAGCGCTCTGTCTGCCTCACCTTTGCCTTCCTCTTCCTGCTGCTGGC  
CATGCTGGTGCAAGCG

146/330

**FIGURE 146**

GGTTCCTACATCCTCTCATCTGAGAATCAGAGAGCATAATCTTCTTACGGGCCCCGTGATTTATTAACGTGGCTT  
AATCTGAAGGTTCTCAGTCAAATTCTTTGTGATCTACTGATTGTGGGGGCATGGCAAGGTTTGCTTAAAGGAGC  
TTGGCTGGTTTTGGGCCCTTGTAGCTGACAGAAGGTGGCCAGGGAGAATGCAGCACACTGCTCGGAGAATGAAGG  
CGCTTCTGTTGCTGGTCTTGCCTTGGCTCAGTCCTGCTAACTACATTGACAATGTGGGCAACCTGCACTTCCTG  
TATTCAGAACTCTGTAAAGGTGCCTCCCACTACGGCCTGACCAAAGATAGGAAGAGGCGCTCACAAGATGGCTG  
TCCAGACGGCTGTGCGAGCCTCACAGCCACGGCTCCCTCCCCAGAGGTTTCTGCAGCTGCCACCATCTCCTTAA  
TGACAGACGAGCCTGGCCTAGACAACCCTGCCTACGTGTCCTCGGCAGAGGACGGGCAGCCAGCAATCAGCCCA  
GTGGACTCTGGCCGGAGCAACCGAACTAGGGCAGGGCCCTTTGAGAGATCCACTATTAGAAGCAGATCATTTAA  
AAAAATAAATCGAGCTTTGAGTGTCTTGAAGGACAAAGAGCGGGAGTGCAGTTGCCAACCATGCCGACCAGG  
GCAGGGAAAATTCTGAAAACACCACTGCCCCTGAAGTCTTTCCAAGGTTGTACCACCTGATTCCAGATGGTGAA  
ATTACCAGCATCAAGATCAATCGAGTAGATCCCAGTGAAAGCCTCTCTATTAGGCTGGTGGGAGGTAGCGAAAC  
CCCCTGGTCCATATCATTATCCAACACATTTATCGTGATGGGGTGATCGCCAGAGACGGCCGGCTACTGCCAG  
GAGACATCATTCTAAAGGTCAACGGGATGGACATCAGCAATGTCCCTCACAACCTACGCTGTGCGTCTCCTGCGG  
CAGCCCTGCCAGGTGCTGTGGCTGACTGTGATGCGTGAACAGAAGTTCGCGAGCAGGAACAATGGACAGGCCCC  
GGATGCCTACAGACCCCCGAGATGACAGCTTTTCATGTGATTCTCAACAAAAGTAGCCCCGAGGAGCAGCTTGAA  
TAAACTGGTGCGCAAGGTGGATGAGCCTGGGGTTTTTCATCTTCAATGTGCTGGATGGCGGTGTGGCATATCGA  
CATGGTCAGCTTGAGGAGAATGACCGTGTGTTAGCCATCAATGGACATGATCTTCGATATGGCAGCCCAGAAAG  
TGCGGCTCATCTGATTACAGGCCAGTGAAAGACGTGTTACCTCGTCGTGTCCCGCCAGGTTCCGGCAGCGGAGCC  
CTGACATCTTTTCAGGAAGCCGGCTGGAACAGCAATGGCAGCTGGTCCCCAGGGCCAGGGGAGAGGAGCAACACT  
CCCAAGCCCCCTCCATCCTACAATTACTTGTGTCATGAGAAGGTGGTAAATATCCAAAAAGACCCCGGTGAATCTCT  
CGGCATGACCGTGCAGGGGGAGCATCACATAGAGAATGGGATTTGCCTATCTATGTCATCAGTGTGAGCCCG  
GAGGAGTCATAAGCAGAGATGGAAGAATAAAAAACAGGTGACATTTTGTGTAATGTGGATGGGGTCGAAC TGACA  
GAGGTGAGCCGGAGTGAGGCAGTGGCATTATTGAAAAGAACATCATCCTCGATAGTACTCAAAGCTTTGGAAGT  
CAAAGAGTATGAGCCCCAGGAAGACTGCAGCAGCCCAGCAGCCCTGGACTCCAACCACAACATGGCCCCACCCA  
GTGACTGGTCCCCATCCTGGGTGATGTGGCTGGAATTACCACGGTGCTTGATAACTGTAAAGATATTGTATTA  
CGAAGAAACACAGCTGGAAGTCTGGGCTTCTGCATTGTAGGAGGTTATGAAGAATACAATGGAAACAAACCTTT  
TTTCATCAAATCCATTGTTGAAGGAACACCAGCATACAATGATGGAAGAATTAGATGTGGTGATATTCTTCTTG  
CTGTCAATGGTAGAAGTACATCAGGAATGATACATGCTTGCTTGGCAAGACTGCTGAAAGAACTTAAAGGAAGA  
ATTACTCTAACTATTGTTTTCTTGGCCTGGCACTTTTTTATAGAAATCAATGATGGGTGAGAGGAAAACAGAAAA  
TCACAAATAGGCTAAGAAGTTGAAACACTATATTTATCTTGTGATTTTTTATATTTAAAGAAAGAATACATTGT  
AAAAATGTCAGGAAAAGTATGATCATCTAATGAAAGCCAGTTACACCTCAGAAAATATGATTCCAAAAAAATTA  
AAACTACTAGTTTTTTTTTTCAGTGTGGAGGATTTCTCATTACTCTACAACATTGTTTATATTTTTTCTATTCAAT  
AAAAAGCCCTAAAACAATAAATGATTGATTTGTATACCCCACTGAATTCAGCTGATTTAAATTTAAATTT  
GGTATATGCTGAAGTCTGCCAAGGGTACATTATGGCCATTTTAAATTTACAGCTAAAATATTTTTTAAATGCA  
TTGCTGAGAAACGTTGCTTTCATCAAACAAGAATAAATATTTTTTCAGAAGTTAAA

147/330

**FIGURE 147**

MKALLLLVLPWLSPANYIDNVGNLHFLYSELCKGASHYGLTKDRKRRSQDGCPDGCASLTAT  
APSPEVSAAATISLMTDEPGLDNPAYVSSAEDGQPAISPVDSGRSNRTRARPFERSTIRSRS  
FKKINRALSVLRRTKSGSAVANHADQGRENSENTTAPEVFPRLYHLIPDGEITSIKINRVDP  
SESLSIRLVGGSETPLVHII IQHIYRDGVIARDGRLLPGDIILKVNGMDISNVPHNYAVRLL  
RQPCQVLWLTVMREQKFRSRNNGQAPDAYRPRDD\$FHVILNKSSPEEQLGIKLVRKVDEPGV  
FIFNVLDGGVAYRHGQLEENDRVLAINGHDLRYGSPESA AHLIQASERRVHLVVSQRQVRQRS  
PDIFQEAGWNSNGSWSPGPGERSNTPKPLHPTITCHEKVVNIQKDPGESLGMTVAGGASHRE  
WDLPIYVISVEPPGGVISRDGRIKTGDILLNVDGVELTEVSRSEAVALLKRTSSSIVLKALEV  
KEYEPQEDCSSPAALDSNHNMAPPSDWSPSWVMWLELPRCLYNCKDIVLRRNTAGSLGFCIV  
GGYEEYNGNKPFFIKSIVEGTPAYNDGRIRCGDILLAVNGRSTSGMIHACLARLLKELKGRI  
TLTIVSWPGTFL



148/330

**FIGURE 148**

CCAAAGTGATCATTTGAAAAAGAGATATCCACATCTTCAAGCCCATATAAAGGATAGAAGCT  
GCACAGGGCAGCTTTACTTACTCCAGCACCTTCCTCTCCCAGGCAA**ATG**GTGCTGACCATCT  
TTGGGATACAATCTCATGGATACGAGGTTTTTAAACATCATCAGCCCAAGCAACAATGGTGGC  
AATG TTCAGGAGACAGTGACAATTGATAATGAAAAAATAACCGCCATCGTTAACATCCATGC  
AGGATCATGCTCTTCTACCACAATTTTTGACTATAAACATGGCTACATTGCATCCAGGGTGC  
TCTCCCGAAGAGCCTGCTTTATCCTGAAGATGGACCATCAGAACATCCCTCCTCTGAACAAT  
CTCCAATGGTACATCTATGAGAAACAGGCTCTGGACAACATGTTCTCCAACAAATACACCTG  
GGTCAAGTACAACCCTCTGGAGTCTCTGATCAAAGACGTGGATTGGTTCCTGCTTGGGTCAC  
CCATTGAGAACTCTGCAAACATATCCCTTTGTATAAGGGGGAAGTGGTTGAAAACACACAT  
AATGTCGGTGCTGGAGGCTGTGCAAAGGCTGGGCTCCTGGGCATCTTGGGAATTTCAATCTG  
TGCAGACATTCATGTT**TAG**GATGATTAGCCCTCTTGTTTTATCTTTTCAAAGAAATACATCC  
TTGGTTTACACTCAAAGTCAAATTAAATTCTTTCCCAATGCCCCAACTAATTTTGAGATTC  
AGTCAGAAAATATAAATGCTGTATTTATA

149/330

**FIGURE 149**

MKILVAFLVVLTIQSHGYEVFNIIISPSNNGGNVQETVTIDNEKNTAIVNIHAGSCSSTT  
IFDYKHGYIASRVLSRRACFILKMDHQNIPLNNLQWYIYEKQALDNMFSNKYTWVKYNPLE  
SLIKDVDWFLLGSPIEKLCKHIPLYKGEVVENTHNVGAGGCAKAGLLGILGISICADIHV

150/330

**FIGURE 150**

GGCACGAGCCAGGAACTAGGAGGTTCTCACTGCCCCGAGCAGAGGCCCTACACCCACCGAGGC  
**ATG**GGGCTCCCTGGGCTGTTCTGCTTGGCCGTGCTGGCTGCCAGCAGCTTCTCCAAGGCACG  
GGAGGAAGAAATTACCCCTGTGGTCTCCATTGCCTACAAAGTCCTGGAAGTTTTCCCCAAAG  
GCCGCTGGGTGCTCATAACCTGCTGTGCACCCCAGCCACCACCGCCCATCACCTATTCCCTC  
TGTGGAACCAAGAACATCAAGGTGGCCAAGAAGGTGGTGAAGACCCACGAGCCGGCCTCCTT  
CAACCTCAACGTCACACTCAAGTCCAGTCCAGACCTGCTCACCTACTTCTGCCGGGCGTCCT  
CCACCTCAGGTGCCCATGTGGACAGTGCCAGGCTACAGATGCACTGGGAGCTGTGGTCCAAG  
CCAGTGTCTGAGCTGCGGGCCAACCTTCACTCTGCAGGACAGAGGGGCAGGCCCCAGGGTGGA  
GATGATCTGCCAGGCGTCCTCGGGCAGCCCACCTATCACCAACAGCCTGATCGGGAAGGATG  
GGCAGGTCCACCTGCAGCAGAGACCATGCCACAGGCAGCCTGCCAACTTCTCCTTCCTGCCG  
AGCCAGACATCGGACTGGTTCTGGTGCCAGGCTGCAAACAACGCCAATGTCCAGCACAGCGC  
CCTCACAGTGGTGCCCCCAGGTGGTGACCAGAAGATGGAGGACTGGCAGGGTCCCCTGGAGA  
GCCCCATCCTTGCCCTTGCCGCTCTACAGGAGCACCCGCCGTCTGAGTGAAGAGGAGTTTGGG  
GGGTTCAGGATAGGGAATGGGGAGGTCAGAGGACGCAAAGCAGCAGCCATG**TAGA**ATGAACC  
GTCCAGAGAGCCAAGCACGGCAGAGGACTGCAGGCCATCAGCGTGCACTGTTTCGTATTTGGA  
GTTTCATGCAAAATGAGTGTGTTTTAGCTGCTCTTGCCACAAAAAAAAAAAAAAAAAAAAA

151/330

**FIGURE 151**

MGLPGLFCLAVLAASSFSKAREEEITPVVSIAYKVLEVFPKGRWVLITCCAPQPPPPITYSL  
CGTKNIKVAKKVVKTHEPASFNLNVTLKSSPDLLTYFCRASSTSGAHVDSARLQMHWELWSK  
PVSELRANFTLQDRGAGPRVEMICQASSGSPITNSLIGKDGQVHLQQRPCHRQPANFSFLP  
SQTSDWFWCQAANNANVQHSALTVVPPGGDQKMEDWQGPLESPIALALPLYRSTRRLSEEEFG  
GFRIGNGEVRGRKAAAM

**Signal Peptide:**

amino acids 1-18

**N-glycosylation Sites:**

amino acids 86-89, 132-135, 181-184

152/330

**FIGURE 152**

GGTCCTTA**ATG**GCAGCAGCCGCCGCTACCAAGATCCTTCTGTGCCTCCCGCTTCTGCTCCTG  
CTGTCCGGCTGGTCCCGGGCTGGGCGAGCCGACCCTCACTCTCTTTGCTATGACATCACCGT  
CATCCCTAAGTTCAGACCTGGACCACGGTGGTGTGCGGTTCAAGGCCAGGTGGATGAAAAGA  
CTTTTCTTCACTATGACTGTGGCAACAAGACAGTCACACCTGTCAGTCCCCTGGGGAAGAAA  
CTAAATGTCACAACGGCCTGGAAAGCACAGAACCCAGTACTGAGAGAGGTGGTGGACATACT  
TACAGAGCAACTGCGTGACATTCAGCTGGAGAATTACACACCCAAGGAACCCCTCACCCCTGC  
AGGCAAGGATGTCTTGTGAGCAGAAAGCTGAAGGACACAGCAGTGGATCTTGGCAGTTCAGT  
TTCGATGGGCAGATCTTCCTCCTCTTTGACTCAGAGAAGAGAATGTGGACAACGGTTCATCC  
TGGAGCCAGAAAGATGAAAGAAAAGTGGGAGAATGACAAGGTTGTGGCCATGTCCTTCCATT  
ACTTCTCAATGGGAGACTGTATAGGATGGCTTGAGGACTTCTTGATGGGCATGGACAGCACC  
CTGGAGCCAAGTGCAGGAGCACCACTCGCCATGTCCTCAGGCACAACCCAACCTCAGGGGCCAC  
AGCCACCACCCTCATCCTTTGCTGCCTCCTCATCATCCTCCCCTGCTTCATCCTCCCTGGCA  
TCTGAGGAGAGTCCTTTAGAGTGACAGGTTAAAGCTGATACCAAAGGCTCCTGTGAGCACG  
GTCTTGATCAAACCTCGCCCTTCTGTCTGGCCAGCTGCCCACGACCTACGGTGTATGTCCAGT  
GGCCTCCAGCAGATCATGATGACATCATGGACCCAATAGCTCATTCACTGCCTTGATTCCCTT  
TTGCCAACAATTTTACCAGCAGTTATACCTAACATATTATGCAATTTTCTCTTGGTGCTACC  
TGATGGAATTCCTGCACTTAAAGTTCTGGCTGACTAAACAAGATATATCATTTTCTTTCTTC  
TCTTTTGTGGAAAATCAAGTACTTCTTTGAATGATGATCTCTTTCTTGCAAATGATATT  
GTCAGTAAAATAATCACGTTAGACTTCAGACCTCTGGGGATTCTTTCCGTGTCCTGAAAGAG  
AATTTTTAAATTATTTAATAAGAAAAAATTTATATTAATGATTGTTTCCTTTAGTAATTTAT  
TGTTCTGTACTGATATTTAAATAAAGAGTTCTATTTCCCAAAAAAAAAAAAAAAAAAAAA

153/330

**FIGURE 153**

MAAAAATKILLCLPLLLLLSGWSRAGRADPHSLCYDITVIPKFRPGPRWCAVQGQVDEKTFL  
HYDCGNKTVTPVSPLGKKLNVTTAWKAQNPVLREVVDILTEQLRDIQLENYTPKEPLTLQAR  
MSCEQKAEGHSSGSWQFSFDGQIFLLFDSEKRMWTTVHPGARKMKEKWENDKVVAMSFHYFS  
MGDCIGWLEDFLMGMDSTLEPSAGAPLAMSSGTTQLRATATTLLILCCLLIILPCFILPGI

**Important features:****Signal peptide:**

amino acids 1-25

**Transmembrane domain:**

amino acids 224-246

**N-glycosylation site.**

amino acids 68-72, 82-86

**N-myristoylation site.**

amino acids 200-206, 210-216

**Amidation site.**

amino acids 77-81

154/330

**FIGURE 154**

GGGAAAGCCATTTTCGAAAACCCATCTATACAACTATATATTTTCATTTCTGCTGCTAGCTG  
CCTTGGGCCTCACAATTTTCATTCTGTTTTCTGACTTTCAAGTTATATACCGTGGA**ATG**GAG  
TTGATCCCAACCATAACATCGTGGAGGGTTTTAATTTTGGTGGTAGCCCTCACCCAATTCTG  
GTGTGGCTTTCTTTGCAGAGGATTCCACCTTCAAAATCATGAACTCTGGCTGTTGATCAAAA  
GAGAATTTGGATTCTACTCTAAAAGTCAATATAGGACTTGGCAAAGAAGCTAGCAGAAGAC  
TCAACCTGGCCTCCCATAAACAGGACAGATTATTCAGGTGATGGCAAAAATGGATTCTACAT  
CAACGGAGGCTATGAAAGCCATGAACAGATTCCAAAAAGAAAACCTCAAATTGGGAGGCCAAC  
CCACAGAACAGCATTTCTGGGCCAGGCTG**TAA**TCAGAATTGTCGTCGTACATGCTCAACAGC  
ATTGCTTTTTTCCCCAAAATTAACACATTGTGGAGAAGTGATGATACTCTCCCCTTACCTTT  
CCTCTCTCCATTCAAGCATTCAAAGTATATTTTCAATGAATTAAACCTTGCAGCAAGGGACC  
TTAGATAGGCTTATTCTGACTGTATGCTTTACCAATGAGAGAAAAAAATGCATTTCTGTAT  
CATCCTTTTCAATAAACTGTATTCATTTTGAAAAAAAAAAAAAAAAAAAAAAAAA

155/330

**FIGURE 155**

MELIPTITSWRVLILVVALTQFWCGFLCRGFHLQNHFWLLIKREFGFYSKSQYRTWQKKLA  
EDSTWPPINRTDYSGDGKNGFYINGGYESHEQIPKRKLKLGGQPTEQHFWARL



156/330

**FIGURE 156**

GTTCTCCTTTCCGAGCCAAAATCCCAGGCGATGGTGAATTATGAACGTGCCACACC**ATGAAG**  
CTCTTGTGGCAGGTAAGTGTGCACCACCACACCTGGAATGCCATCCTGCTCCCGTTTCGTCTA  
CCTCACGGCGCAAGTGTGGATTCTGTGTGCAGCCATCGCTGCTGCCGCCTCAGCCGGGCCCC  
AGAACTGCCCCCTCCGTTTGCTCGTGCAGTAACCAGTTTCAAGCAAGGTGGTGTGCACGCGCCGG  
GGCCTCTCCGAGGTCCCGCAGGGTATTCCCTCGAACACCCGGTACCTCAACCTCATGGAGAA  
CAACATCCAGATGATCCAGGCCGACACCTTCCGCCACCTCCACCACCTGGAGGTCTTGCAGT  
TGGGCAGGAACTCCATCCGGCAGATTGAGGTGGGGGCCTTCAACGGCCTGGCCAGCCTCAAC  
ACCCTGGAGCTGTTTCGACAACTGGCTGACAGTCATCCCTAGCGGGGCCTTTGAATACCTGTC  
CAAGCTGCGGGAGCTCTGGCTTCGCAACAACCCCATCGAAAGCATCCCCTCTTACGCCTTCA  
ACCGGGTGGCCTCCCTCATGCGCCTGGACTTGGGGGAGCTCAAGAAGCTGGAGTATATCTCT  
GAGGGAGCTTTTGAGGGGCTGTTCAACCTCAAGTATCTGAACTTGGGCATGTGCAACATTAA  
AGACATGCCCAATCTCACCCCCCTGGTGGGGCTGGAGGAGCTGGAGATGTGAGGGAACCACT  
TCCCTGAGATCAGGCCTGGCTCCTTCCATGGCCTGAGCTCCCTCAAGAAGCTCTGGGTCTATG  
AACTCACAGGTCAGCCTGATTGAGCGGAATGCTTTTGACGGGCTGGCTTCACTTGTGGAAGT  
CAACTTGGCCCACAATAACCTCTCTTCTTTGCCCCATGACCTCTTTACCCCGCTGAGGTACC  
TGGTGGAGTTGCATCTACACCACAACCTTGGAACTGTGATTGTGACATTCTGTGGCTAGCC  
TGGTGGCTTCGAGAGTATATACCCACCAATTCCACCTGCTGTGGCCGCTGTCATGCTCCCAT  
GCACATGCGAGGCCGCTACCTCGTGGAGGTGGACCAGGCCTCCTTCCAGTGCTCTGCCCCCT  
TCATCATGGACGCACCTCGAGACCTCAACATTTCTGAGGGTTCGGATGGCAGAACTTAAGTGT  
CGGACTCCCCCTATGTCTCCTCCGTGAAGTGGTTGCTGCCCAATGGGACAGTGCTCAGCCACGC  
CTCCCGCCACCCAAGGATCTCTGTCTCAACGACGGCACCTTGAACCTTTTCCACGTGCTGC  
TTTCAGACACTGGGGTGTACACATGCATGGTGACCAATGTTGCAGGCAACTCCAACGCCTCG  
GCCTACCTCAATGTGAGCACGGCTGAGCTTAACACCTCCAACCTACAGCTTCTTACCACAGT  
AACAGTGGAGACCACGGAGATCTCGCCTGAGGACACAACGCGAAAGTACAAGCCTGTTCTTA  
CCACGTCCACTGGTTACCAGCCGGCATATACACCTCTACCACGGTGCTCATTACAGACTACC  
CGTGTGCCCAAGCAGGTGGCAGTACCCGCGACAGACACCACTGACAAGATGCAGACCAGCCT  
GGATGAAGTCATGAAGACCACCAAGATCATCATTGGCTGCTTTGTGGCAGTGACTCTGCTAG  
CTGCCGCCATGTTGATTGTCTTCTATAAACTTCGTAAGCGGCACCAGCAGCGGAGTACAGTC  
ACAGCCGCCCCGACTGTTGAGATAATCCAGGTGGACGAAGACATCCCAGCAGCAACATCCGC  
AGCAGCAACAGCAGCTCCGTCCGGTGTATCAGGTGAGGGGGCAGTAGTGCTGCCCACAATTC  
ATGACCATATTAACATAACACCTACAAACCAGCACATGGGGCCCACTGGACAGAAAACAGC  
CTGGGGAACTCTCTGCACCCACAGTCACCACTATCTCTGAACCTTATATAATTACAGACCA  
TACCAAGGACAAGGTACAGGAACTCAAATA**TGA**CTCCCCTCCCCCAAAAACTTATAAAAT  
GCAATAGAATGCACACAAAGACAGCAACTTTTGTACAGAGTGGGGAGAGACTTTTTCTTGTA  
TATGCTTATATATTAAGTCTATGGGCTGGTTAAAAAAAACAGATTATATTAAATTTAAAGA  
CAAAAAGTCAAAACA

157/330

**FIGURE 157**

MKLLWQVTVHHHTWNAILLPFVYLTAQVWILCAAIAAAASAGPQNCPSVCSCSNQFSKVVCT  
RRGLSEVPQGIPSNTRYLNLMENNIQMIQADTFRHLHHLEVLQLGRNSIRQIEVGAFNGLAS  
LNTLELFDNWLTVIPSGAFEYLSKLRRLWLRNNPIESIPSYAFNRVP SLMRLDLGELKKLEY  
ISEGAFEGLEFNLKYLNLGMCNIKDMPNLTPLVGLEELEM SGNHFPEIRPGSFHGLSSLKKLW  
VMNSQVSLIERNAFDGLASLVELNLAHNNLSSLP HDLFTPLRYLVELHLHHNPWNCD CDILW  
LAWWLREYIPTNSTCCGRCHAPMHMRGRYLVEVDQASFQCSAPFIMDAPRDLNISEGRMAEL  
KCRTPPMSSSVKWLLPNGTVLSHASRHPRISVLNDGT LNF SHVLLSDTGVYTCMVTNVAGNSN  
ASAYLNVSTAELNTSNYSFFT TTVTVETTEISPEDTTRKYKPVPTTSTGYQPAYTTSTTVLIQ  
TTRVPKQVAVPATD TTDKMQTS LDEVMKTTKIIIGCFVAVTLLAAAMLIVFYKLRKRHQQRS  
TVTAARTVEIIQVDEDI PAATSAAATAAPSGVSGEGAVVLPTIHDHINYNTYKPAHGAHWTE  
NSLGNLHPTVTTISEPYIIQTHTKDKVQETQI

**FIGURE 158**

[illegible]

159/330

**FIGURE 159**

MELGCWTQLGLTFLQLLLISSLPREYTVINEACPGAENIMCRECCEYDQIECVCPGKREVV  
GYTIPCCRNEENECDSCLIHPGCTIFENCKSCRNGSWGGLDDFYVKGIFYCAECRAGWYGGD  
CMRCGQVLRAPKGQILLESYPLNAHCEWTIHAKPGFVIQLRFVMLSLEFDYMCQYDYVEVRD  
GDNRDGQIIKRVCGNERPAPIQSIGSSLHVLFSHSDGSKNFDGFAIYEEITACSSSPCFHDG  
TCVLDKAGSYKCACLAGYTGQRCENLLEERNCSDPGGPVNGYQKITGGPGLINGRHAKIGTV  
VSFFCNNSYVLSGNEKRTCQQNGEWSGKQPICIKACREPKISDLVRRRVLPQVQSRETPLH  
QLYSAAFSKQKLQSAPTKKPALPFGDLPMGYQHLHTQLQYECISPFYRRLGSSRRTCLRTGK  
WSGRAPSCIPICGKIENITAPKTQGLRWPWQAAIYRRTSGVHDGSLHKGAWFLVCSGALVNE  
RTVVVAAHCVTDLGKVTMIKTADLKVVLGKFYRDDDRDEKTIQSLQISAILHPNYDPILLD  
ADIAILKLLDKARISTRVQPICLAASRDLSTSFQESHITVAGWNVLADVRS PGFKNDTLRSG  
VVSVDSSLCEEQHEDHGIPVSVTDNMFCASWEPTAPSDICTAETGGIAAVSFPGRASPEPR  
WHLMGLVSWSYDKTCSHRLSTAFTKVLPFKDWIERNMK

160/330

**FIGURE 160**

ACCAGGCATTGTATCTTCAGTTGTCATCAAGTTCGCAATCAGATTGGAAAAGCTCAACTTGA  
AGCTTTCTTGCCTGCAGTGAAGCAGAGAGATAGATATTATTACGTAATAAAAAACATGGGC  
TTCAACCTGACTTTCCACCTTTCCCTACAAATTCGATTACTGTTGCTGTTGACTTTGTGCCT  
GACAGTGGTTGGGTGGGCCACCAGTAACTACTTCGTGGGTGCCATTCAAGAGATTCCTAAAG  
CAAAGGAGTTCATGGCTAATTTCCATAAGACCCTCATTTTGGGGAAGGGAAAAACTCTGACT  
AATGAAGCATCCACGAAGAAGGTAGAACTTGACAACTGTCCTTCTGTGTCTCCTTACCTCAG  
AGGCCAGAGCAAGCTCATTTTCAAACCAGATCTCACTTTGGAAGAGGTACAGGCAGAAAATC  
CCAAAGTGTCCAGAGGCCGGTATCGCCCTCAGGAATGTAAAGCTTTACAGAGGGTCGCCATC  
CTCGTTCCCCACCGGAACAGAGAGAAACACCTGATGTACCTGCTGGAACATCTGCATCCCTT  
CCTGCAGAGGCAGCAGCTGGATTATGGCATCTACGTCATCCACCAGGCTGAAGGTAAAAAGT  
TTAATCGAGCCAACTCTTGAATGTGGGCTATCTAGAAGCCCTCAAGGAAGAAAATTGGGAC  
TGCTTTATATTCCACGATGTGGACCTGGTACCCGAGAATGACTTTAACCTTTACAAGTGTGA  
GGAGCATCCCAAGCATCTGGTGGTTGGCAGGAACAGCACTGGGTACAGGTTACGTTACAGTG  
GATATTTTGGGGGTGTTACTGCCCTAAGCAGAGAGCAGTTTTTCAAGGTGAATGGATTCTCT  
AACAACTACTGGGGATGGGGAGGCGAAGACGATGACCTCAGACTCAGGGTTGAGCTCCAAAG  
AATGAAAATTTCCCGGCCCTGCCTGAAGTGGGTAAATATACAATGGTCTTCCACACTAGAG  
ACAAAGGCAATGAGGTGAACGCAGAACGGATGAAGCTCTTACACCAAGTGTACAGAGTCTGG  
AGAACAGATGGGTTGAGTAGTTGTTCTTATAAATTAGTATCTGTGGAACACAATCCTTTATA  
TATCAACATCACAGTGGATTTCTGGTTTGGTGCATGACCCTGGATCTTTTGGTGATGTTTGG  
AAGAACTGATTCTTTGTTTGCAATAATTTTGGCCTAGAGACTTCAAATAGTAGCACACATTA  
AGAACCTGTTACAGCTCATTGTTGAGCTGAATTTTTCCTTTTTGTATTTTCTTAGCAGAGCT  
CCTGGTGATGTAGAGTATAAAACAGTTGTAACAAGACAGCTTCTTAGTCATTTTGATCATG  
AGGGTTAAATATTGTAATATGGTACTTGAAGGACTTTATATAAAAGGATGACTCAAAGGAT  
AAAATGAACGCTATTTGAGGACTCTGGTTGAAGGAGATTTATTTAAATTTGAAGTAATATAT  
TATGGGATAAAAGGCCACAGGAAATAAGACTGCTGAATGTCTGAGAGAACCAGAGTTGTTCT  
CGTCCAAGGTAGAAAGGTACGAAGATACAATACTGTTATTCATTTATCCTGTACAATCATCT  
GTGAAGTGGTGGTGTGAGGTGAGAAGGCGTCCACAAAAGAGGGGAGAAAAGGCGACGAATCA  
GGACACAGTGAACCTGGGAATGAAGAGGTAGCAGGAGGGTGGAGTGTGCGCTGCAAAGGCAG  
CAGTAGCTGAGCTGGTTGCAGGTGCTGATAGCCTTCAGGGGAGGACCTGCCCAGGTATGCCT  
TCCAGTGATGCCCACCAGAGAATACATTCTCTATTAGTTTTTAAAGAGTTTTTGTAAAATGA  
TTTTGTACAAGTAGGATATGAATTAGCAGTTTACAAGTTTACATATTAATAATAATAATA  
TGTCTATCAAATACCTCTGTAGTAAAATGTGAAAAGCAAAA

161/330

**FIGURE 161**

MGFNLT FHLSYKFRLLLLLTLCLTVVGWATSNYFVGAIQEIPKAKEFMANFHKTLILGKGKT  
LTNEASTKKVELDNCPSVSPYLRGQSKLIFKPDLTLEEVQAENPKVSRGRYRPQECKALQRV  
AILVPHRNREKHLMYLLEHLHPFLQRQQLDYGIYVIHQAEKGKFNRAKLLNVGYLEALKEEN  
WDCFIFHDVDLVPENDFNLYKCEEHPKHLVVGGRNSTGYRLRYSGYFGGVTALSREQFFKVNG  
FSNNYWGWGGEDDDLRLRVELQRMKISRPLPEVGKYTMVFHTRDKGNEVNAERMKLLHQVSR  
VWRTDGLSSCSYKLVSVEHNPLYINITVDFWFGA

**Important features:****Signal peptide:**

amino acids 1-27

**N-glycosylation sites:**

amino acids 4-7, 220-223 and 335-338

**Xylose isomerase proteins:**

amino acids 191-201

162/330

**FIGURE 162**

CGTGGGCCGGGGTCGCGCAGCGGGCTGTGGGCGCGCCCGGAGGAGCGACCGCCGCAGTTCTC  
GAGCTCCAGCTGCATTCCCTCCGCGTCCGCCCCACGCTTCTCCCGCTCCGGGCCCCGCA**ATG**  
GCCCAGGCAGTGTGGTCGCGCCTCGGCCGCATCCTCTGGCTTGCCTGCCTCCTGCCCTGGGC  
CCCGGCAGGGGTGGCCGCAGGCCTGTATGAACTCAATCTCACCACCGATAGCCCTGCCACCA  
CGGGAGCGGTGGTGACCATCTCGGCCAGCCTGGTGGCCAAGGACAACGGCAGCCTGGCCCTG  
CCCGCTGACGCCCACCTCTACCGCTTCCACTGGATCCACACCCCGCTGGTGTCTACTGGCAA  
GATGGAGAAGGGTCTCAGCTCCACCATCCGTGTGGTTCGGCCACGTGCCCGGGGAATTCCCGG  
TCTCTGTCTGGGTCACTGCCGCTGACTGCTGGATGTGCCAGCCTGTGGCCAGGGGCTTTGTG  
GTCCTCCCCATCACAGAGTTCCCTCGTGGGGGACCTTGTTGTCACCCAGAACACTTCCCTACC  
CTGGCCCAGCTCCTATCTCACTAAGACCGTCCTGAAAGTCTCCTTCTCCTCCACGACCCGA  
GCAACTTCCCTCAAGACCGCCTTGTTTCTCTACAGCTGGGACTTCGGGGACGGGACCCAGATG  
GTGACTGAAGACTCCGTGGTCTATTATAACTATTCCATCATCGGGACCTTCACCGTGAAGCT  
CAAAGTGGTGGCGGAGTGGGAAGAGGTGGAGCCGGATGCCACGAGGGGCTGTGAAGCAGAAGA  
CCGGGGACTTCTCCGCCTCGCTGAAGCTGCAGGAAACCCTTCGAGGCATCCAAGTGTGGGG  
CCCACCCTAATTACAGACCTTCCAAAAGATGACCGTGACCTTGAACCTTCTGGGGAGCCCTCC  
TCTGACTGTGTGCTGGCGTCTCAAGCCTGAGTGCCTCCCGCTGGAGGAAGGGGAGTGCCACC  
CTGTGTCCGTGGCCAGCACAGCGTACAACCTGACCCACACCTTCAGGGACCTTGGGGACTAC  
TGCTTCAGCATCCGGGGCCGAGAATATCATCAGCAAGACACATCAGTACCACAAGATCCAGGT  
GTGGCCCTCCAGAATCCAGCCGGCTGTCTTTGCTTTCCCATGTGCTACACTTATCACTGTGA  
TGTTGGCCTTCATCATGTACATGACCCTGCGGAATGCCACTCAGCAAAAGGACATGGTGGAG  
AACCCGGAGCCACCCTCTGGGGTCAAGTGCTGCTGCCAGATGTGCTGTGGGCCTTTCTTGCT  
GGAGACTCCATCTGAGTACCTGGAAATTGTTCTGTGAGAACACGGGCTGCTCCCGCCCCCTCT  
ATAAGTCTGTCAAACTTACACCGTG**TGA**GCACTCCCCCTCCCCACCCCATCTCAGTGTTAA  
CTGACTGCTGACTTGGAGTTTCCAGCAGGGTGGTGTGCACCACTGACCAGGAGGGGTTTATT  
TGCGTGGGGCTGTTGGCCTGGATCATCCATCCATCTGTACAGTTCAGCCACTGCCACAAGCC  
CCTCCCTCTCTGTACCCCTGACCCCAAGCATTACCCATCTGTACAGTCCAGCCACTGACA  
TAAGCCCCACTCGGTTACCACCCCTTGACCCCTACCTTTGAAGAGGCTTCGTGCAGGACT  
TTGATGCTTGGGGTGTTCGCTGTGACTCCTAGGTGGGCCTGGCTGCCCACTGCCCATTCCT  
CTCATATTGGCACATCTGCTGTCCATTGGGGGTTCTCAGTTTCTCCTCCCCCAGACAGCCCTAC  
CTGTGCCAGAGAGCTAGAAAGAAGGTCATAAAGGGTTAAAAATCCATAACTAAAGGTTGTAC  
ACATAGATGGGCACACTCACAGAGAGAAGTGTGCATGTACACACACCACACACACACACA  
CACACACACACAGAAATATAAACACATGCGTCACATGGGCATTTAGATGATCAGCTCTGTA  
TCTGGTTAAGTCGGTTGCTGGGATGCACCCTGCACTAGAGCTGAAAGGAAATTTGACCTCCA  
AGCAGCCCTGACAGGTTCTGGGCCCCGGGCCCTCCCTTTGTGCTTTGTCTCTGCAGTTCTTGC  
GCCCTTTATAAGGCCATCCTAGTCCCTGCTGGCTGGCAGGGGCTGGATGGGGGGCAGGACT  
AATACTGAGTGATTGCAGAGTGCTTTATAAATATCACCTTATTTTATCGAAACCCATCTGTG  
AAACTTTCACTGAGGAAAAGGCCTTGACGCGGTAGAAGAGGTTGAGTCAAGGCCGGGCGCGG  
TGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGTGGATCACGAGATCAGGA  
GATCGAGACCACCCTGGCTAACACGGTGAAACCCCGTCTCTACTAAAAAATAACAAAAGTT  
AGCCGGGCGTGGTGGTGGTGCCTGTAGTCCCAGCTACTCGGGAGGCTGAGGCAGGAGAATG  
GTGCGAACCCGGGAGGCGGAGCTTGCACTGAGCCAGATGGCGCCACTGCACTCCAGCCTGA  
GTGACAGAGCGAGACTCTGTCTCCA

163/330

**FIGURE 163**

MAQAVWSRLGRILWLACLLPWAPAGVAAGLYELNLTTDSPATTGAVVTISASLVAKDNGSLA  
LPADAHLYRFHWIHTPLVLTGKMEKGLSSTIRVVGHVPGEFPVSVWVTAADCWMCQPVARGF  
VVLPITEFLVGDLVVTQNTSLPWPSYLTKTVLKVSFLLHDPSNFLKTALFLYSWDFGDGTQ  
MVTEDSVVYYNYSIIGTFTVKLKVVAEWEEVEPDATRAVKQKTGDFSASLKLQETLRGIQVL  
GPTLIQTFQKMTVTNLNFLGSPPLTVCWRLKPECLPLEEGECHPVSVASTAYNLTHTFRDPGD  
YCFSIRAENIISKTHQYHKIQVWPSRIQPAVFAFPCATLITVMLAFIMYMTLRNATQQKDMV  
ENPEPPSGVRCCCQMCCGPFLLETPSEYLEIVRENHGLLPPLYKSVKTYTV

**Important features of the protein:****Signal peptide:**

amino acids 1-24

**Transmembrane domain:**

amino acids 339-362

**N-glycosylation sites.**

amino acids 34-37, 58-61, 142-145, 197-200, 300-303 and 364-367





165/330

**FIGURE 165**

MALSSQIWAACLLLLLLLLASLTSGSVFPQQTGQLAELQPQDRAGARASWMPMFQRRRRRDTH  
FPICIFCCGCCHRSKCGMCCKT

166/330

**FIGURE 166**

CTGTCAGGAAGGACCATCTGAAGGCTGCAATTTGTTCTTAGGGAGGCAGGTGCTGGCCTGGC  
CTGGATCTTCCACC**ATG**TTCCCTGTTGCTGCCTTTTGATAGCCTGATTGTCAACCTTCTGGGC  
ATCTCCCTGACTGTCCTCTTCACCCTCCTTCTCGTTTTTCATCATAGTGCCAGCCATTTTTTG  
AGTCTCCTTTGGTATCCGCAAACCTCTACATGAAAAGTCTGTTAAAAATCTTTGCGTGGGCTA  
CCTTGAGAATGGAGCGAGGAGCCAAGGAGAAGAACCACCAGCTTTACAAGCCCTACACCAAC  
GGAATCATTGCAAAGGATCCCACCTCACTAGAAGAAGAGATCAAAGAGATTTCGTCTGAAGTGG  
TAGTAGTAAGGCTCTGGACAACACTCCAGAGTTCGAGCTCTCTGACATTTTCTACTTTTGCC  
GGAAAGGAATGGAGACCATTATGGATGATGAGGTGACAAAGAGATTCTCAGCAGAAGAACTG  
GAGTCCTGGAACCTGCTGAGCAGAACCAATTATAACTTCCAGTACATCAGCCTTCGGCTCAC  
GGTCCTGTGGGGGTTAGGAGTGCTGATTTCGGTACTGCTTTCTGCTGCCGCTCAGGATAGCAC  
TGGCTTTCACAGGGATTAGCCTTCTGGTGGTGGGCACAACTGTGGTGGGATACTTGCCAAAT  
GGGAGGTTTAAGGAATTCATGAGTAAACATGTTCACTTAATGTGTTACCGGATCTGCGTGCG  
AGCGCTGACAGCCATCATCACCTACCATGACAGGGAAAACAGACCAAGAAATGGTGGCATCT  
GTGTGGCCAATCATACCTCACCGATCGATGTGATCATCTTGGCCAGCGATGGCTATTATGCC  
ATGGTGGGTCAAGTGCACGGGGGACTCATGGGTGTGATTTCAGAGAGCCATGGTGAAGGCCTG  
CCCACACGTCTGGTTTGAGCGCTCGGAAGTGAAGGATCGCCACCTGGTGGCTAAGAGACTGA  
CTGAACATGTGCAAGATAAAAGCAAGCTGCCTATCCTCATCTTCCCAGAAGGAACCTGCATC  
AATAATACATCGGTGATGATGTTCAAAAAGGGAAGTTTTTGAAATTGGAGCCACAGTTTACCC  
TGTTGCTATCAAGTATGACCCTCAATTTGGCGATGCCTTCTGGAACAGCAGCAAATACGGGA  
TGGTGACGTACCTGCTGCGAATGATGACCAGCTGGGCCATTGTCTGCAGCGTGTGGTACCTG  
CCTCCCATGACTAGAGAGGCAGATGAAGATGCTGTCCAGTTTGCGAATAGGGTGAAATCTGC  
CATTGCCAGGCAGGGAGGACTTGTGGACCTGCTGTGGGATGGGGGCTGAAGAGGGAGAAGG  
TGAAGGACACGTTCAAGGAGGAGCAGCAGAAGCTGTACAGCAAGATGATCGTGGGGAACCAC  
AAGGACAGGAGCCGCTCC**TGA**GCCTGCCTCCAGCTGGCTGGGGCCACCGTGCGGGGTGCCAA  
CGGGCTCAGAGCTGGAGTTGCCGCCGCCGCCCCCACTGCTGTGTCCTTTCCAGACTCCAGGG  
CTCCCCGGGCTGCTCTGGATCCCAGGACTCCGGCTTTCGCCGAGCCGCAGCGGGATCCCTGT  
GCACCCGGCGCAGCCTACCCTTGGTGGTCTAAACGGATGCTGCTGGGTGTTGCGACCCAGGA  
CGAGATGCCTTGTTTCTTTTACAATAAGTCGTTGGAGGAATGCCATTAAAGTGAACCTCCCA  
CCTTTGCACGCTGTGCGGGCTGAGTGGTTGGGGAGATGTGGCCATGGTCTTGTGCTAGAGAT  
GGCGGTACAAGAGTCTGTTATGCAAGCCCGTGTGCCAGGGATGTGCTGGGGGCGGCCACCCG  
CTCTCCAGGAAAGGCACAGCTGAGGCACTGTGGCTGGCTTCGGCCTCAACATCGCCCCCAGC  
CTTGAGCTCTGCAGACATGATAGGAAGGAAACTGTCATCTGCAGGGGCTTTCAGCAAAATG  
AAGGGTTAGATTTTTTATGCTGCTGCTGATGGGGTTACTAAAGGGAGGGGAAGAGGCCAGGTG  
GGCCGCTGACTGGGCCATGGGGAGAACGTGTGTTCTGCTACTCCAGGCTAACCCTGAACCTCCC  
ATGTGATGCGCGCTTTGTTGAATGTGTGTCTCGGTTTCCCCATCTGTAATATGAGTCGGGGG  
GAATGGTGGTGATTCCCTACCTCACAGGGCTGTTGTGGGGATTAAAGTGCTGCGGGTGAGTGA  
AGGACACATCACGTTCAAGTACAGGCCACAAAACGGGGCACGGCAGGCCTGAG  
CTCAGAGCTGCTGCACTGGGCTTTGGATTTGTTCTTGTGAGTAAATAAACTGGCTGGTGAA  
TGA

167/330

**FIGURE 167**

MFLLLPFDSLIVNLLGISLTVLFTLLLVFIIIVPAIFGVVSFGIRKLYMKSLLKIFAWATLRME  
RGAKEKNHQLYKPYTNGIIAKDPTSLEEEIKEIRRS GSSKALDNTPEFELSDIFYFCRKGME  
TIMDDEVTKRFSAAEELESWNLLSRTNYNFQYISLRRLTVLWGLGVLIRYCFLPLRIALAFTG  
ISLLVVGTTVVGYPNGRFKEFMSKHVHLMCYRICVRALTAIITYHDRENRP RNGGICVANH  
TSPIDV IILASDGYAMVGQVHGGLMGVIQ RAMVKACPHVWFERSEVKDRHLVAKRLTEHVQ  
DKSKLPILIFPEGTCINNTSVMMFKKGSFEIGATVYPVAIKYDPQFGDAFWNSSKYGMV TYL  
LRMMTSWAIVCSVWYLP PMTREADEDAVQFANRVKSAIARQGGLVDLLWDGGLKREKV KDTF  
KEEQQKLYSKMIVGNHKDRSRS

168/330

**FIGURE 168**

GCCCCCTCGAAACCAGGACTCCAGCACCTCTGGTCCCGCCCTCACCCGGACCCCTGGCCCTCA  
CGTCTCCTCCAGGG**ATG**GCGCTGGCGGCTTTGATGATCGCCCTCGGCAGCCTCGGCCTCCAC  
ACCTGGCAGGCCCAGGCTGTTCCCACCATCCTGCCCCCTGGGCCTGGCTCCAGACACCTTTGA  
CGATACCTATGTGGGTTGTGCAGAGGAGATGGAGGAGAAGGCAGCCCCCTGCTAAAGGAGG  
AAATGGCCCACCATGCCCTGCTGCGGGAATCCTGGGAGGCAGCCCAGGAGACCTGGGAGGAC  
AAGCGTCGAGGGCTTACCTTGCCCCCTGGCTTCAAAGCCCAGAATGGAATAGCCATTATGGT  
CTACACCAACTCATCGAACACCTTGTACTGGGAGTTGAATCAGGCCGTGCGGACGGGCGGAG  
GCTCCCGGGAGCTCTACATGAGGCACTTTCCCTTCAAGGCCCTGCATTTCTACCTGATCCGG  
GCCCTGCAGCTGCTGCGAGGCAGTGGGGGCTGCAGCAGGGGACCTGGGGAGGTGGTGTTCG  
AGGTGTGGGCAGCCTTCGCTTTGAACCCAAGAGGCTGGGGGACTCTGTCCGCTTGGGCCAGT  
TTGCCTCCAGCTCCCTGGATAAGGCAGTGGCCACAGATTTGGGGAGAAGAGGCGGGGCTGT  
GTGTCTGCGCCAGGGGTGCAGCTAGGGTCACAATCTGAGGGGGCCTCCTCTGCCCCCCTG  
GAAGACTCTGCTCTTGCCCCCTGGAGAGTTCCAGCTCTCAGGGGTTGGGCCCT**TGA**AAGTCCA  
ACATCTGCCACTTAGGAGCCCTGGGAACGGGTGACCTTCATATGACGAAGAGGCACCTCCAG  
CAGCCTTGAGAAGCAAGAACATGGTTCCGGACCCAGCCCTAGCAGCCTTCTCCCCAACCAGG  
ATGTTGGCCTGGGGAGGCCACAGCAGGGCTGAGGGAACTCTGCTATGTGATGGGGACTTCCT  
GGGACAAGCAAGGAAAGTACTGAGGCAGCCACTTGATTGAACGGTGTTGCAATGTGGAGACA  
TGGAGTTTTATTGAGGTAGCTACGTGATTAAATGGTATTGCAGTGTGGA

169/330

**FIGURE 169**

MALAALMIALGSLGLHTWQAQAVPTILPLGLAPDTFDDTYVGCAEEMEEKAAPLLKEEMAHH  
ALLRESWEAAQETWEDKRRGLTLPPGFKAQNGIAIMVYTNSSNTLYWELNQAVRTGGGSREL  
YMRHFPPFKALHFYLIRALQLLRGSGGCSRGPGEVVFRGVGSLRFEPKRLGDSVRLGQFASS  
LDKAVAHRFGEKRRGCVSAPGVQLGSQSEGASSLPPWKTLLLAPGEFQLSGVGP

170/330

**FIGURE 170**

GTGGCTTCATTT CAGTGGCTGACTTCCAGAGAGCAAT**ATG**GCTGGTTCCCCAACATGCCTCA  
CCCTCATCTATATCCTTTGGCAGCTCACAGGGTCAGCAGCCTCTGGACCCGTGAAAGAGCTG  
GTCGGTTCCGTTGGTGGGGCCGTGACTTTCCCCCTGAAGTCCAAAGTAAAGCAAGTTGACTC  
TATTGTCTGGACCTTCAACACAACCCCTCTTGTACCATAACAGCCAGAAGGGGGCACTATCA  
TAGTGACCCAAAATCGTAATAGGGAGAGAGTAGACTTCCCAGATGGAGGCTACTCCCTGAAG  
CTCAGCAAACCTGAAGAAGAATGACTCAGGGATCTACTATGTGGGGATATACAGCTCATCACT  
CCAGCAGCCCTCCACCCAGGAGTACGTGCTGCATGTCTACGAGCACCTGTCAAAGCCTAAAG  
TCACCATGGGTCTGCAGAGCAATAAGAATGGCACCTGTGTGACCAATCTGACATGCTGCATG  
GAACATGGGGAAGAGGATGTGATTTATACCTGGAAGGCCCTGGGGCAAGCAGCCAATGAGTC  
CCATAATGGGTCCATCCTCCCCATCTCCTGGAGATGGGGAGAAAGTGATATGACCTTCATCT  
GCGTTGCCAGGAACCCTGTCAGCAGAACTTCTCAAGCCCCATCCTTGCCAGGAAGCTCTGT  
GAAGGTGCTGCTGATGACCCAGATTCCCTCCATGGTCCTCCTGTGTCTCCTGTTGGTGCCCCT  
CCTGCTCAGTCTCTTTGTACTGGGGCTATTTCTTTGGTTTCTGAAGAGAGAGAGACAAGAAG  
AGTACATTGAAGAGAAGAAGAGAGTGGACATTTGTCTGGGAAACTCCTAACATATGCCCCCAT  
TCTGGAGAGAACACAGAGTACGACACAATCCCTCACACTAATAGAACAATCCTAAAGGAAGA  
TCCAGCAAATACGGTTTACTCCACTGTGGAAATACCGAAAAAGATGGAAAATCCCCACTCAC  
TGCTCACGATGCCAGACACACCAAGGCTATTTGCCTATGAGAATGTTATC**TAG**ACAGCAGTG  
CACTCCCCTAAGTCTCTGCTCA

171/330

**FIGURE 171**

MAGSPTCLTLIYILWQLTGSAASGPVKELVGSVGGAVTFPLKSKVKQVDSIVWTFNTTPLVT  
IQPEGGTIIIVTQNRNRERVDFPDGGYSLKLSKLKKNDSGIYYVGIYSSSLQQPSTQEYVLHV  
YEHLSPKPKVTMGLQSNKNGTCVTNLTCCMEHGEEDEVITYWKALGQAANESHNGSILPISWRW  
GESDMTFICVARNPVSRNFSSPILARKLCEGAADDPDSSMVLLCLLLVPLLLSLFVLGLFLW  
FLKRERQEEYIEEKKRVDICRETPNICPHSGENTHEYDTIPHTNRTILKEDPANTVYSTVEIP  
KKMENPHSLLTMPDTPRLFAYENVI



172/330

**FIGURE 172**

CTGGTTCCCCAACATGCCTCACCCCTCATCTATATCCTTTGGCAGCTCACAGGGTCAGCAGCC  
TCTGGACCCCGTGAAAGAGCTGGTCGGTTCCGTTGGTGGGGCCGTGACTTTCCCCCTGAAGTC  
CAAAGTAAAGCAAGTTGACTCTATTGTCTGGACCTTCAACACAACCCCTCTTGTCACCATAC  
AGCCAGAAGGGGGCACTATCATAGTGACCCAAAATCGTAATAGGGAGAGAGTAGACTTCCCA  
GATGGAGGGCTACTCCCTGAAGCTCAGCAAACCTGAAGAAGAATGACTCAGGGATCTACTATGT  
GGGGATATACAGCTCATCACTCCAGCAGCCCTCCACCCAGGAGTACGTGCTGCATGTCTACG  
AGCACCTGTCAAAGCCTAAAGTCACCATGGGTCTGCAGAGCAATAAGAATGGCACCTGTGTG  
ACCAATCTGACATGCTGCATGGAACATGGGGAAGAGGATGTGATTTATACCTGGAAGGCCCT  
GGGGCAAGCAGCCAATGAGTCCCATAATGGGTCCATCCTCCCCATCTCCTGGAGATGGGGAG  
AAAGTGATATGACCTTCATCTGCGTTGCCAGGAACCCTGTCAGCAGAACTTCTCAAGCCCC  
ATCCTTGCCAGGAAGCTCTGTGAAGGTGCTGCTGATGACCCAGATTCCCTCCATGGTCCTCCT  
GTGTCTCCTGTTGGTGCCCCCTCCTGCTCAGTCTCTTTGTACTGGGGCTATTTCTTTGGTTTC  
TGAAGAGAGAGAGACAAGAAGAGTACATTGAAGAGAAGAAGAGAGTGGACATTTGTCTGGGAA  
ACTCCTAACATATGCCCCCATTCTGGAGAGAACACAGAGTACGACACAATCCCTCACACTAA  
TAGAACAATCCTAAAGGAAGATCCAGCAAATACGGTTTACTCCACTGTGGAAATACCGAAAA  
AGATGGAAAATCCCCACTCACTGCTCACGATGCCAGACACACCAAGGCTATTTGCCTATGAG  
AATGTTATCTAGACAGCAGTGCCTCCCCTAAGTCTCTGCTCAAAAAAAAAAAAAAAAAAAAAA

173/330

**FIGURE 173**

GAAAGACGTGGTCCTGACAGACAGACAATCCTATTCCCTACCAAA**ATGA**AGATGCTGCTGCT  
GCTGTGTTTGGGACTGACCCTAGTCTGTGTCCATGCAGAAGAAGCTAGTTCTACGGGAAGGA  
ACTTTAATGTAGAAAAGATTAATGGGGAATGGCATACTATTATCCTGGCCTCTGACAAAAGA  
GAAAAGATAGAAGAACATGGCAACTTTAGACTTTTTCTGGAGCAAATCCATGTCTTGGAGAA  
TTCCTTAGTTCTTAAAGTCCATACTGTAAGAGATGAAGAGTGCTCCGAATTATCTATGGTTG  
CTGACAAAACAGAAAAGGCTGGTGAATATTCTGTGACGTATGATGGATTCAATACATTTACT  
ATACCTAAGACAGACTATGATAACTTTCTTATGGCTCACCTCATTAACGAAAAGGATGGGGA  
AACCTTCCAGCTGATGGGGCTCTATGGCCGAGAACCAGATTTGAGTTCAGACATCAAGGAAA  
GGTTTGCACAACTATGTGAGGAGCATGGAATCCTTAGAGAAAATATCATTTGACCTATCCAAT  
GCCAATCGCTGCCTCCAGGCCCGAGAATGAAGAATGGCCTGAGCCTCCAGTGTTGAGTGGAC  
ACTTCTCACCAGGACTCCACCATCATCCCTTCCTATCCATACAGCATCCCCAGTATAAATTC  
TGTGATCTGCATTCCATCCTGTCTCACTGAGAAGTCCAATTCAGTCTATCAACATGTTACC  
TAGGATACCTCATCAAGAATCAAAGACTTCTTTAAATTTCTCTTTGATACACCCTTGACAAT  
TTTTCATGAAATTATTCCTCTTCCTGTTCAATAAATGATTACCCTTGCACTTAA

174/330

**FIGURE 174**

MKMLLLLCGLTLVCVHAEEASSTGRNFNVEKINGEWHTIILASDKREKIEEHG NFR LFLEQ  
IHVLENSLV LKVHTVRDEECSELSMVADKTEKAGEYSVTYDGFNTFTIPKTDYDNFLMAHLI  
NEKDGETFQLMGLYGREPDLSSDIKERFAQLCEEHGILRENIIDLSNANRCLQARE

175/330

**FIGURE 175**

GGCTCGAGCGTTTCTGAGCCAGGGGTGACC**ATG**ACCTGCTGCGAAGGATGGACATCCTGCAA  
TGGATTCAGCCTGCTGGTTCTACTGCTGTTAGGAGTAGTTCTCAATGCGATACCTCTAATTG  
TCAGCTTAGTTGAGGAAGACCAATTTTCTCAAACCCCATCTCTTGCTTTGAGTGGTGGTTC  
CCAGGAATTATAGGAGCAGGTCTGATGGCCATTCCAGCAACAACAATGTCCTTGACAGCAAG  
AAAAAGAGCGTGCTGCAACAACAGAACTGGAATGTTTCTTTCATCATTTTTTCAGTGTGATCA  
CAGTCATTGGTGCTCTGTATTGCATGCTGATATCCATCCAGGCTCTCTTAAAAGGTCCTCTC  
ATGTGTAATTCTCCAAGCAACAGTAATGCCAATTGTGAATTTTCATTGAAAAACATCAGTGA  
CATTTCATCCAGAATCCTTCAACTTGCAGTGGTTTTTCAATGACTCTTGTGCACCTCCTACTG  
GTTTCAATAAACCCACCAGTAACGACACCATGGCGAGTGGCTGGAGAGC**AT**CTAGTTTCCAC  
TTCGATTCTGAAGAAAACAAACATAGGCTTATCCACTTCTCAGTATTTTTAGGTCTATTGCT  
TGTTGGAATTCTGGAGGTCCTGTTTGGGCTCAGTCAGATAGTCATCGGTTTCCTTGGCTGTC  
TGTGTGGAGTCTCTAAGCGAAGAAGTCAAATTGTG**TAG**TTTAATGGGAATAAAATGTAAGTA  
TCAGTAGTTTGAAAAAAAAAAAA

176/330

**FIGURE 176**

MTCCEGWTSCNGFSLLVLLLLGVVLNAIPLIVSLVEEDQFSQNPISCFEWWFPGIIGAGLMA  
IPATTMSLTARKKRACCNNRTGMFLSSFFSVITVIGALYCMLISIQALLKGPLMCNSPSNSNA  
NCEFSLKNISDIHPESFNLQWFFNDSCAPPTGFNKPTSNDTMASGWRASSFHFDSEENKHRL  
IHFSVFLGLLLVGILEVLFGLSQIVIGFLGCLCGVSKRRSQIV

177/330

**FIGURE 177**

GTCGAATCCAAATCACTCATTGTGAAAGCTGAGCTCACAGCCGAATAAGCCACC**ATG**AGGCT  
GTCAGTGTGTCTCCTGATGGTCTCGCTGGCCCTTTGCTGCTACCAGGCCCATGCTCTTGTCT  
GCCCAGCTGTTGCTTCTGAGATCACAGTCTTCTTATTCTTAAGTGACGCTGCGGTAAACCTC  
CAAGTTGCCAAACTTAATCCACCTCCAGAAGCTCTTGCAGCCAAGTTGGAAGTGAAGCACTG  
CACCGATCAGATATCTTTTAAGAAACGACTCTCATTGAAAAAGTCCTGGTGGAAA**TAG**TGAA  
AAAATGTGGTGTGTGACATGTAAAAATGCTCAACCTGGTTTCCAAAGTCTTTCAACGACACC  
CTGATCTTCACTAAAAATTGTAAAGGTTTCAACACGTTGCTTTAATAAATCACTTGCCCTGC

178/330

**FIGURE 178**

MRLSVCLLMVSLALCCYQAHALVCPAVASEITVFLFLSDAAVNLQVAKLNPPPEALAAKLEV  
KHCTDQISFKKRLSLKKSWWK

179/330

**FIGURE 179**

ATCCGTTCTCTGCGCTGCCAGCTCAGGTGAGCCCTCGCCAAGGTGACCTCGCAGGACACTGG  
TGAAGGAGCAGTGAGGAACCTGCAGAGTCACACAGTTGCTGACCAATTGAGCTGTGAGCCTG  
GAGCAGATCCGTGGGCTGCAGACCCCCGCCCCAGTGCCTCTCCCCCTGCAGCCCTGCCCCCTC  
GAACTGTGACATGGAGAGAGTGACCCTGGCCCTTCTCCTACTGGCAGGCCTGACTGCCTTGG  
AAGCCAATGACCCATTTGCCAATAAAGACGATCCCTTCTACTATGACTGGAAAAACCTGCAG  
CTGAGCGGACTGATCTGCGGAGGGCTCCTGGCCATTGCTGGGATCGCGGCAGTTCTGAGTGG  
CAAATGCAAATACAAGAGCAGCCAGAAGCAGCACAGTCCTGTACCTGAGAAGGCCATCCCAC  
TCATCACTCCAGGCTCTGCCACTACTTGCTTGAGCACAGGACTGGCCTCCAGGGATGGCCTGA  
AGCCTAACACTGGCCCCCAGCACCTCCTCCCCTGGGAGGCCTTATCCTCAAGGAAGGACTTC  
TCTCCAAGGGCAGGCTGTTAGGCCCTTTCTGATCAGGAGGCTTCTTTATGAATTAACTCG  
CCCCACCACCCCCTCA



180/330

**FIGURE 180**

MERVTLALLLLAGLTALEANDPFANKDDPFYYDWKNLQLSGLICGGLLAIAGIAAVLSGKCK  
YKSSQKQHSPVPEKAIPLITPGSATTC

181/330

**FIGURE 181**

GGAGAAGAGGTTGTGTGGGACAAGCTGCTCCCGACAGAAGG**ATG**TCGCTGCTGAGCCTGCCC  
TGGCTGGGCCTCAGACCGGTGGCAATGTCCCCATGGCTACTCCTGCTGCTGGTTGTGGGCTC  
CTGGCTACTCGCCCGCATCCTGGCTTGGACCTATGCCTTCTATAACAACCTGCCGCCGGCTCC  
AGTGTTTTCCACAGCCCCCAAACGGAACTGGTTTTGGGGTCACCTGGGCCTGATCACTCCT  
ACAGAGGAGGGCTTGAAGGACTCGACCCAGATGTCGGCCACCTATTCCCAGGGCTTTACGGT  
ATGGCTGGGTCCCATCATCCCCTTCATCGTTTTATGCCACCCTGACACCATCCGGTCTATCA  
CCAATGCCTCAGCTGCCATTGCACCCAAGGATAATCTCTTCATCAGGTTCCCTGAAGCCCTGG  
CTGGGAGAAGGGATACTGCTGAGTGGCGGTGACAAGTGGAGCCGCCACCGTCGGATGCTGAC  
GCCCCGCTTCCATTTCAACATCCTGAAGTCCTATATAACGATCTTCAACAAGAGTGCAAACA  
TCATGCTTGACAAGTGGCAGCACCTGGCCTCAGAGGGCAGCAGTCGTCTGGACATGTTTGAG  
CACATCAGCCTCATGACCTTGGACAGTCTACAGAAATGCATCTTCAGCTTTGACAGCCATTG  
TCAGGAGAGGCCCAGTGAATATATTGCCACCATCTTGGAGCTCAGTGCCCTTGTAGAGAAAA  
GAAGCCAGCATATCCTCCAGCACATGGACTTTCTGTATTACCTCTCCCATGACGGGCGGCGC  
TTCCACAGGGCCTGCCGCTGGTGCATGACTTCACAGACGCTGTCATCCGGGAGCGGCGTCG  
CACCTCCCCACTCAGGGTATTGATGATTTTTTCAAAGACAAAGCCAAGTCCAAGACTTTGG  
ATTTCAATTGATGTGCTTCTGCTGAGCAAGGATGAAGATGGGAAGGCATTGTCAGATGAGGAT  
ATAAGAGCAGAGGCTGACACCTTCATGTTTGGAGGCCATGACACCACGGCCAGTGGCCTCTC  
CTGGGTCTGTACAACCTTGCGAGGCACCCAGAATACCAGGAGCGCTGCCGACAGGAGGTGC  
AAGAGCTTCTGAAGGACCGGATCCTAAAGAGATTGAATGGGACGACCTGGCCCAGCTGCCC  
TTCCTGACCATGTGCGTGAAGGAGAGCCTGAGGTTACATCCCCCAGCTCCCTTCATCTCCCG  
ATGCTGCACCCAGGACATTGTTCTCCAGATGGCCGAGTCATCCCAAAGGCATTACCTGCC  
TCATCGATATTATAGGGGTCCATCACAACCCA~~ACT~~GTGTGGCCGGATCCTGAGGTCTACGAC  
CCCTTCCGCTTTGACCCAGAGAACAGCAAGGGGAGGTACCTCTGGCTTTTATTCCCTTTCTC  
CGCAGGGCCCAGGAACTGCATCGGGCAGGCGTTGCCATGGCGGAGATGAAAGTGGTCCTGG  
CGTTGATGCTGCTGCACTTCCGGTTCCTGCCAGACCACACTGAGCCCCGAGGAAGCTGGAA  
TTGATCATGCGCGCCGAGGGCGGGCTTTGGCTGCGGGTGGAGCCCCTGAATGTAGGCTTGCA  
**GTGA**CTTTCTGACCCATCCACCTGTTTTTTTTGCAGATTGTCATGAATAAAACGGTGCTGTCAA

182/330

**FIGURE 182**

MSLLSLPWLGLRPVAMSPWLLLLLVVGSWLLARILAWTYAFYNNCRRLQCFPQPPKRNWFWG  
HLGLITPTEEGLKDSTQMSATYSQGFTVWLGPIIPFIVLCHPDTIRSITNASAAIAPKDNLF  
IRFLKPWLGE GILLSGGDKWSRHRRLTPAFHFNILKSYITIFNKSANIMLDKWQHLASEGS  
SRLDMFEHISLMTLDSLQKCIFSFDSHCQERPSEYIATILELSALVEKRSQHILQHMDFLYY  
LSHDGRRFHRACRLVHDFTDAVIRERRRTLPTQGIDDFKDKAKSKTLD FIDVLLLSKDEDG  
KALSDEDIRAEADTFMFGGHDTTASGLSWVLYNLARHPEYQERCQEVQELLKDRDPKEIEW  
DDLAQLPFLTMCVKESLRLHPPAPFISRCCTQDIVLPDGRVIPKGITCLIDIIGVHHNPTVW  
PDPEVYDPFRFDPENSKGRSPLAFIPFSAGPRNCIGQAFAMAEMKVVLALMLLHFRFLPDHT  
EPRRKLELIMRAEGGLWLRVEPLNVGLQ

183/330

**FIGURE 183**

CAACAGAAGCCAAGAAGGAAGCCGTCTATCTTGTGGCGATC**ATG**TATAAGCTGGCCTCCTGC  
TGTTTGCTTTTCACAGGATTCTTAAATCCTCTCTTATCTCTTCCTCTCCTTGACTCCAGGGA  
AATATCCTTTCAACTCTCAGCACCTCATGAAGACGCGCGCTTAACTCCGGAGGAGCTAGAAA  
GAGCTTCCTTCTACAGATATTGCCAGAGATGCTGGGTGCAGAAAGAGGGGATATTCTCAGG  
AAAGCAGACTCAAGTACCAACATTTTTTAACCCAAGAGGAAATTTGAGAAAGTTTCAGGATTT  
CTCTGGACAAGATCCTAACATTTTACTGAGTCATCTTTTGGCCAGAATCTGGAAACCATACA  
AGAAACGTGAGACTCCTGATTGCTTCTGGAAATACTGTGTC**TGA**AGTGAAATAAGCATCTGT  
TAGTCAGCTCAGAAACACCCATCTTAGAATATGAAAAATAACACAATGCTTGATTTGAAAAC  
AGTGTGGAGAAAAACTAGGCAAACTACACCCTGTTTCATTGTTACCTGGAAAATAAATCCTCT  
ATGTTTTGCACAAAAAAAAAAAAAAAAA

184/330

**FIGURE 184**

MYKLASCCLLFTGFLNPLLSLPLLDREISFQLSAPHEDARLTPEELERASLLQILPEMLGA  
ERGDILRKADSSTNIFNPRGNLRKFQDFSGQDPNILLSHLLARIWKPYKKRETPDCFWKYCV

185/330

**FIGURE 185**

GAACATTTTTAGTTCCCAAGGAATGTACATCAGCCCCACGGAAGCTAGGCCACCTCTGGGAT  
GGGGTTGCTGGTTTAAAACAAACGCCAGTCATCCTATATAAGGACCTGACAGCCACCAGGCA  
CCACCTCCGCCAGGAAGTGCAGGCCCCACCTGTCTGCAACCCAGCTGAGGCC**ATG**CCCTCCCC  
AGGGACCGTCTGCAGCCTCCTGCTCCTCGGCATGCTCTGGCTGGACTTGGCCATGGCAGGCT  
CCAGCTTCCTGAGCCCTGAACACCAGAGAGTCCAGCAGAGAAAGGAGTCGAAGAAGCCACCA  
GCCAAGCTGCAGCCCCGAGCTCTAGCAGGCTGGCTCCGCCCCGGAAGATGGAGGTCAAGCAGA  
AGGGGCAGAGGATGAACTGGAAGTCCGGTTCAACGCCCCCTTTGATGTTGGAATCAAGCTGT  
CAGGGGTTTCAGTACCAGCAGCACAGCCAGGCCCTGGGGAAGTTTCTTCAGGACATCCTCTGG  
GAAGAGGCCAAAGAGGCCCCAGCCGACAAG**TGA**TCGCCCAACAAGCCTTACTCACCTCTCTCT  
AAGTTTAGAAGCGCTCATCTGGCTTTTCGCTTGCTTCTGCAGCAACTCCCACGACTGTTGTA  
CAAGCTCAGGAGGCGAATAAATGTTCAAACCTGTA

186/330

**FIGURE 186**

MPSPGTVCSLLLLGMLWLDLAMAGSSFLSPEHQRVQQRKESKKPPAKLQPRALAGWLRPEDG  
GQAEGAEDELEVRFNAPFDVGIKLSGVQYQQHSQALGKFLQDILWEEAKEAPADKO

187/330

**FIGURE 187**

CGGCCACAGCTGGCATGCTCTGCCTGATCGCCATCCTGCTGTATGTCCTCGTCCAGTACCTC  
GTGAACCCCGGGGTGCTCCGCACGGACCCCAGATGTCAAGAAT**ATGA**ACACGTGGCTGCTGT  
TCCTCCCCCTGTTCCCGGTGCAGGTGCAGACCCTGATAGTCGTGATCATCGGGATGCTCGTG  
CTCCTGCTGGACTTTCTTGGCTTGGTGCACCTGGGCCAGCTGCTCATCTTCCACATCTACCT  
GAGTATGTCCCCCACCCTAAGCCCCCGATCCCCCAAGGCTGGGTGGTCAGAGCTGCTCATC  
TTACACCTCTACTTGAGTATGTCCCTAACCCTGAGCCCCCAGCCTGGGGCCAGAGTCTTT  
GTCCCCCGTGTGCGCATGTGTTTCAGGGTCAGCCTCTCCCAGAAGTGAGATCATGGACAAAAA  
GGGCAAATCACAGGAAGAAATTAAATCCATGAGGACCCAGCAGGCCCCAGCAAGAAGCTGAAC  
TCACGCCGAGACCTGCAGGAGTGGTGCCAGGTGCT**TGA**AGTAACAAGTTTAAATGTTTCAGA  
GACAATGGAATGGAATCTATTAGGCAAGAACAGGACATTATGAAATAAGGACAGGTGGACTT  
CCAAAAACACAAGTAGAAATTCTAACAATGAAATATATTACAGGCAGGTACCCACTAACCA  
AACAACTGAAGCGAGAGCTGTGGTCTTGCTTGGTCTCACAGTGGGCACAGCGGTAGGCGGTC  
AGTCATGTTGCTGAACGACGGAGGGTAAACTCCCCAGCCCCAAGAAAACCTGTGTTGGAAGT  
AACAAACACCTCCCTGCTCCTGGCACCCAGCCGTTTTGGTCATGGTGGGCCAGCTGCAAAGCG  
TCTTCCATTCTCTGGGCAGTGGTGGCCCCGAGGCTGTGGCCTCTCAGGGGGTTTCTGTGGAC  
ACGGGCAGCAGAGTGTGTCCAGGCCAGCCCCAAGAATGCCCTGCTCCTGACAGCTTGGCCA  
ACCCCTGGTCAGGGCAGAGGGAGTTGGGTGGGTGAGGCTCTGGGCTCACCTCCATCTCCAGA  
GCATCCCCTGCCTGCAGTTGTGGCAAGAACGCCCAGCTCAGAATGAACACACCCCAACCAAGA  
GCCTCCTTGTTTCATAACCACAGGTTACCCTACAAACCACTGTCCCCACACAACCCTGGGGAT  
GTTTTTAAACACACACCTCTAACGCATATCTTACAGTCACTGTTGTCTTGCCTGAGGGTTGA  
ATTTTTTTTTAATGAAAGTGCAATGAAAATCACTGGATTAAATCCTACGGACACAGAGCTGAA  
AAAAAAAAAAAAAAAAAAAAAAAAAAAAA



188/330

**FIGURE 188**

MNTWLLFLPLFPVQVQTLIVVIIGMLVLLLDLGLVHLGQLLIFHIYLSMSPTLSPRSPQGW  
VVRAAHLTPLLEYVPNPEPPTPGARVFVPRVRMCSGSASPRSEIMDKKGKSQEEIKSMRTQQ  
AQQEAELTPRPAGVPGA

189/330

**FIGURE 189**

GGAGTGCAGATGGCATCCTTCGGTTCTTCCAGACAAGCTGCAAGACGCTGACC**ATG**GCCAAG  
ATGGAGCTCTCGAAGGCCTTCTCTGGCCAGCGGACACTCCTATCTGCCATCCTCAGCATGCT  
ATCACTCAGCTTCTCCACAACATCCCTGCTCAGCAACTACTGGTTTGTGGGCACACAGAAGG  
TGCCCAAGCCCCTGTGCGAGAAAGGTCTGGCAGCCAAGTGCTTTGACATGCCAGTGTCCCTG  
GATGGAGATACCAACACATCCACCCAGGAGGTGGTACAATACAACCTGGGAGACTGGGGATGA  
CCGGTTCTCCTTCCGGAGCTTCCGGAGTGGCATGTGGCTATCCTGTGAGGAAACTGTGGAAG  
AACCAGGGGAGAGGTGCCGAAGTTTCATTGAACTTACACCACCAGCCAAGAGAGGTGAGAAA  
GGACTACTGGAATTTGCCACGTTGCAAGGCCCATGTCACCCCACTCTCCGATTTGGAGGGAA  
GCGGTTGATGGAGAAGGCTTCCCTCCCCTCCCCTCCCCTGGGGCTTTGTGGCAAAAATCCTA  
TGGTTATCCCTGGGAACGCAGATCACCTACATCGGACTTCAATTCATCAGCTTCCTCCTGCT  
ACTAACAGACTTGCTACTCACTGGGAACCCTGCCTGTGGGCTCAAACCTGAGCGCCTTTGCTG  
CTGTTTCCTCTGTCCTGTCAGGTCTCCTGGGGATGGTGGCCACATGATGTATTCAACAAGTC  
TTCCAAGCGACTGTCAACTTGGGTCCAGAAGACTGGAGACCACATGTTTGGAATTATGGCTG  
GGCCTTCTACATGGCCTGGCTCTCCTTCACCTGCTGCATGGCGTCGGCTGTCACCACCTTCA  
ACACGTACACCAGGATGGTGCTGGAGTTCAAGTGCAAGCA**TAG**TAAGAGCTTCAAGGAAAAC  
CCGAAGTGCCTACCACATCACCATCAGTGTTTCCCTCGGCGGCTGTCAAGTGCAGCCCCCAC  
CGTGGGTCCTTTGACCAGCTACCACCAGTATCATAATCAGCCCATCCACTCTGTCTCTGAGG  
GAGTCGACTTCTACTCCGAGCTGCGGAACAAGGGATTTCAAAGAGGGGCCAGCCAGGAGCTG  
AAAGAAGCAGTTAGGTCATCTGTAGAGGAAGAGCAGTGTTAGGAGTTAAGCGGGTTTGGGGA  
GTAGGCTTGAGCCCTACCTTACACGTCTGCTGATTATCAACATGTGCTTAAGCCAACATCCG  
TCTCTTGAGCATGGTTTTTTAGAGGCTACGAATAAGGCTATGAATAAGGGTTATCTTTAAGTC  
CTAAGGGATTCTTGGGTGCCACTGCTCTCTTTTCTCTACAGCTCCATCTTGTTTCACCCAC  
CCCACATCTCACACATCCAGAATTCCTTCTTTACTGATAGTTTCTGTGCCAGGTTCTGGGC  
TAAACCATGGAGATAAAAAGAAGAGTAAAATACACTTCCCGACCTTAAGGATCTGAAA

190/330

**FIGURE 190**

MAKMELSKAFSGQRTLLSAILSMLSLSFSTTSLLSNYWFVGTQKVPKPLCEKGLAAKCFDMP  
VSLDGD TNTSTQEVVQYNWETGDDRFSFRSFRSGMWLSCEETVEEPGERCRSFIELTPPAKR  
GEKGLLEFATLQGPCHPTLRFGGKRLMEKASLPSPPLGLCGKNPMVIPGNADHLHRTSIHQL  
PPATNRLATHWEPCLWAQTERLCCCFLCPVRSPGDGGPHDVFTSLPSCQLGSRRLTTCLE  
LWLGLLHGLALLHLLHGVGCHHLQHVHQDGAGVQVQA

191/330

**FIGURE 191**

AACTGGAAGGAAAGAAAGAAAGGTCAGCTTTGGCCCAG**ATG**TGGTTACCCCTTGGTCTCCTG  
TCTTTATGTCTTTCTCCTCTTCCTATTCTGTCATCTCCCTCACTTAAGTCTCAGGCCTGTCA  
GCAGCTCCTGTGGACATTGCCATCCCCTCTGGTAGCCTTCAGAGCAAACAGGACAACCTATG  
TTATGGATGTTTCCACCAACCAGGGTAGTGGCATGGAGCACCGTAACCATCTGTGCTTCTGT  
GATCTCTATGACAGAGCCACTTCTCCACCTCTGAAATGTTCCCTGCTCTGAAATCTGGCATG  
AGATGGCACAGGTGACCACGCAGAAGCCACCAGAATCTTGCCTGCCCTATTCTCCTCCCAA  
GTCTGTTCTCTTATTGTCAACCTCAGCACAAACAGGCTGGCGCCAATGGCATTACAGAGAAAG  
CAATCTGTGTGGCTAGTGGGCAGATTACCATGCAAGCCCCAGGAGAAATGGAGGAGCTTTGT  
AGCCACCTCCCTGTGTCAGCCAGTATTAACATGTCCCCTTCCCCCTGCCCCGCCGTAGATTGAG  
GACATTCGCCCCCTGTGTGCCACCAAACCAGGACTTTCCCCTTGGCTTGGCATCCCTGGCTCT  
CTCCTGGTACCCAGCAAGACGTCTGTTCCAGGGCAGTGTAGCATCTTTCAAGCTCCGTTACT  
ATGGCGATGGCCATGATGTTACAATCCCCTTGCCTGAATAATCAAGTGGGAAGGGGAAGCA  
GAGGGAAATGGGGCCATGTGAATGCAGCTGCTCTGTTCTCCCTACCCTGAGGAAAAACCAAA  
GGGAAGCAACAGGAACTTCTGCAACTGGTTTTTATCGGAAAGATCATCCTGCCTGCAGATGC  
TGTTGAAGGGGCACAAGAAATGTAGCTGGAGAAGATTGATGAAAGTGCAGGTGTGTAAGGAA  
ATAGAACAGTCTGCTGGGAGTCAGACCTGGAATTCTGATTCCAACTCTTTATTACTTTGGG  
AAGTCACTCAGCCTCCCCGTAGCCATCTCCAGGGTGACGGAACCCAGTGTATTACCTGCTGG  
AACCAAGGAAACTAACAATGTAGGTTACTAGTGAATACCCCAATGGTTTCTCCAATTATGCC  
CATGCCACCAAAACAATAAAACAAAATTCTCTAACACTGAAA

192/330

**FIGURE 192**

MWLPLGLLSLCLSPILSSPSLKSQACQQLLWTLPSPLVAFRANRTTYVMDVSTNQSGME  
HRNHLCFCDLYDRATSPPLKCSLL

193/330

**FIGURE 193**

GTAGCGCGTCTTGGGTCTCCCGGCTGCCGCTGCTGCCGCCGCCGCTCGGGTCGTGGAGCCAGGAGCGACGTCA  
CCGCC**ATGGC**AGGCATCAAAGCTTTGATTAGTTTGTCTTTGGAGGAGCAATCGGACTGATGTTTTTGATGCTT  
GGATGTGCCCTTCCAATATACAACAAATACTGGCCCCCTCTTTGTTCTATTTTTTTACATCCTTTCACCTATTCC  
ATACTGCATAGCAAGAAGATTAGTGGATGATACAGATGCTATGAGTAACGCTTGTAAGGAACCTTGCCATCTTTC  
TTACAACGGGCATTGTCTGTCTCAGCTTTTGGACTCCCTATTGTATTTGCCAGAGCACATCTGATTGAGTGGGGA  
GCTTGTGCACTTGTCTCACAGGAAACACAGTCATCTTTGCAACTATACTAGGCTTTTTCTTGGTCTTTGGAAG  
CAATGACGACTTCAGCTGGCAGCAGTGG**TGAA**AAAGAAATTACTGAACTATTGTCAAATGGACTTCCTGTCAATTT  
GTTGGCCATTACGCACACAGGAGATGGGGCAGTTAATGCTGAATGGTATAGCAAGCCTCTTGGGGGTATTTTA  
GGTGCTCCCTTCTCACTTTTATTGTAAGCATACTATTTTCACAGAGACTTGCTGAAGGATTAAAAGGATTTTCT  
CTTTTGAAAAGCTTGACTGATTTACACTTATCTATAGTATGCTTTTTGTGGTGTCTGCTGAATTTAAATAT  
TTATGTGTTTTCTGTAGGTTGATTTTTTTTGGGAATCAATATGCAATGTTAAACACTTTTTTAATGTAATCA  
TTTGCATTGGTTAGGAATTCAGAATTCGCGCCGGCTCTATTACTGGTCAAGTACATCTTTTCTCTTAAATATT  
TAGCCTCCATTATTACAAAAAATTATAAAAAATAAGTTTTCAGTCAGTCAGGATGACATCACTCCCAATGTTATG  
CAGACATACAGACGGTTGGCATACTGTTATAGACTGTATACTCAGTGCAAATATAGCTGCATTTATACCTCAGAG  
GGGCCAAGTGTTAATGCCCATGCCCTCCGTTAAGGGTTGTTGGTTTTACTGGTAGACAGATGTTTTGTGGATTG  
AAAATTATTTTATGGAATTGCTACAGAGGAGTGCTTTTCTTCTCAATTGTTAGAAGAATTTATGTTAACTTTA  
AGGTAAGGGTGTA AAAACATTTTTGAGATAAGGTTTTTATTTATGTTTATTATTGTTAGAGTGAGTTGCAATG  
GGGAAGAAATGACATTGAAATTCAGTTTTTGAATCCTGTTTCTATTTATAAGTGAAATTTGTGATCTCCTATC  
AACCTTTCATGTTTTACCCTGTTAAATGGACATACATGGAACCACTACTGATGAGGGACAGTTGTATGTTTGC  
ATCATATATGCCAGAAAACCTTCCTCTGCTTCCTCCTTTTGACTTATTTGGTATGTTGTATATATTACATAAAA  
TAACTTTTCAAATATAGTTTAATAACACTTAGAAGTGTTTACTTACCTGGAAAATAATTGCTATGCCGTACATT  
CAGAGTGCCCCCTCCCCTGCAAGGCCTTGCCATGATTAACAAGTAACCTTGTTAGTCTTACAGATAATTCAATGCA  
TTAACAGTTTAAGATTTAGACCATGGTAATAGTAGTTCTTATTCTCTAAGGTTATATCATATGTAATTTAAAG  
TATTTTAAAGACAAGTTTCCTGTATACCTCTGAACGTGTTTTGATTTTGAGTTCATCATGATAGATCTGCTGTTT  
CCTTATAAAAGGCATTTGTTGTGTGAGTTAATGCAAAGTAGCCAAGTCCAGCTATATAGCAGCTTCAGAAACAT  
ACCTGACCAAAAAATTTCCAGTAACCAGGCATGATCAATTTATAGTGGTCGTTTACATCTAATAATTATCAGGA  
CTTTTTTCAGGAGTGGGTTATAAAAAACATTCAAGTTGGTCTGACAGTATTTTGTTAAGGATATTTGTTTGTATG  
TTTATTCAGTATACTTACATAAAAAATTATTTGCCATCAGCCAAAACCTCAGTAATCATGACAGCTGTCTGTTGT  
TTTATGAAGTTTATTTCTCAAGAAAAATGGGAATAAATTTGGGATTTGTTTCAGCTTTTTTTACTAAAGATGCCTAA  
AGCCACAGGTTTTATTGCCTAACTTAAGCCATGACTTTTAGATATGAGATGACGGGAAGCAGGACGAAATATCG  
GCGTGTGGCTGGAGCCTTCCCACTGGAGGCTGAAAGTGGCTTGTGGTATTATAATGTTTCAGATTTCAAGAGGAA  
GGTGCAGGTACACATGAGTTAGAGAGCTGGTGAGACAGTTGGGAACCTTTGTGCTTGTGATCTACTGGACTTT  
TTTTTTGCAGGAAGTGCATTCTCTGGTCCCTCCCTATTTTCTGTTCTGGATGTCAGTGCAGTGCAGTGCCTACTG  
TTTTATCCACTTGGCCACAGACTTTTTCTAACAGCTGCGTATTATTTCTATATACTAATTGCATTGGCAGCATT  
GTGTCTTTGACCTTGATACTAGCTTGACATAGTGCTGTCTCTGATTTCTAGGCTAGTTACTTGAGATATGAAT  
TTTCCATAGAATATGCACTGATACAACATTACCATTCTTCTATGGAAAGAAAACCTTTTGATGATGAAACAATAA  
AGATTTTAAATATCTATTTTAAAAA

194/330

**FIGURE 194**

MAGIKALISLSFGGAIGLMFLMLGCALPIYNKYWPLFVLFFYILSPIPYCIARRLVDDTDAM  
SNACKELAIFLTGTGIVVSAFGLPIVFARAHLEWGACALVLTGNTVIFATILGFFLVFGSND  
DFSWQQW

**FIGURE 195**

CCACGCGTCCGCCACGCGTCCGCCACGCGTCCGCCACGCGTCCGCCACGCGTCCGCCACGCGTCCGCC  
CACGCGTCCGGTCAAGCTCGCGCCGCACACTGCTGGTGGAGGGAAGGAGCCCGGGCGCTCTCGCCGCTCCC  
CGCGCGCGCGTCCGACCTCCCAACCGCCCGCCCGCCCGCCCGCCCGCCGCAAGCATGAGTGAGCCCGCT  
TCTGCAGCTGCCCGGGGCGCAATGGCAGGCTGTTTCCGCGGAGTAAAGGTGGCGCGGTCAGTGGTGGTTT  
CAATGACGGACATTAACGACAGTGCAGATCCTGGGGAGTCGCGAGCGCCCGAGTTTGGAGTTTTTCCCCC  
AACGTCAAGTCCGAATGCAGAGGAAAGGAGCGAGGAGGCAAGCTCGGGCTCCGCGACGTAGTTGG  
GAACTTGGGGTCTAGAAGTGCCTCCCCCGCTTGGCGCGCCCTTGACGCCCGAGCCGAGCAGCAAGT  
GAGACATTGTGCGCTGCCAGATCCGCGCGCGCGGACCGGGCTGCCTCGGAAACACAGAGGGGTCTTCTCT  
GCCCTGCATATAATTAGCTGCACAAAGGAGCAGCTGAATGGAGTTGTCACTCTCGAAAGAGGATTTCT  
GACCGAGCGCTTCCAATGGACATTCTCCAGTCTCTCTGAAAGATTCTCGTAATGGATTTCCTGCTCGGT  
CTCTGTCTATACATGGCTGCTGAGGAGGCGCTCGGGGTGGTCTTGTGTCTGCTGGGGGCTGCTTTCAGATGCT  
GCCCGCGCGCCCGAGCGGGTGCCCGAGCTGTGCGGTGCGAGGGGCGGCTGCTGTACTGCGAGGCGCTCAACC  
TCACCGAGGCGCCCCACAACCTGTCCGGCTGCTGGGCTTGTCCCTGCGCTACAACAGCCTCTCGGAGCTGCG  
GCCGCGCAGTTACAGGGGTAAATGCAGCTCACGTGGCTCTATCTGGATACAATCACATCTGCTCCGTGCAGGG  
GGACGCTTTAGCAAACTGCGCCGAGTTAAGGAACCTCACGTGAGTTCCAACAGCATACCCCAACTGCCAAC  
CCACCTTCGGGCCCATGCCAACCTGCGCAGCGTGGACCTCTCGTACAACAAGCTGACGGCGCTCGCGCCGAC  
CTCTTCCACGGGCTGCGGAAGCTCACACGCTGCATATGCGGGCCAACGCCATCCAGTTTGTGCCGTGCGCAT  
CTTCCAGGACTCGCGCAGCCTCAAGTTTCTGCACATCGGATACAATCAGCTCAAGAGTCTGGCGCGCAACTCTT  
TCGCCGGCTTGTTTAAAGCTACCGAGCTGCACCTCGAGCAACAAGCTTGGTCAAGGTGAACCTCGCCACTTC  
CCGCGCCTCATCTCCCTGCACTCGCTCTGCTTGGGAGGAACAAGGTGGCCATTGTGGTCAGCTCGCTGGACTG  
GGTTTGGAACTTGGAGAAATGGACTTGTGCGGCAACGAGATCGAGTACATGGAGCCCCATGTGTTTCGAGACCG  
TGCCGCACTTGCAGTCCCTGCAGCTGGACTCCAACCGCTCACCTACATCGAGCCCGGATCTCAACTCTTGG  
AAGTCCCTGACAAGCATCACCTTGGCGGGGAACCTGTGGGATTGCGGGCGCAACGTGTGTGCCCTAGCCTCGTG  
GCTCAGCAACTTCAGGGGCGCTACGATGGCAACTTGCAGTGCAGCGAGCCCGGATACGCACAGGGCGGAGGACG  
TCTTGGACGCGGTGTACGCTTCCACCTGTGCGAGGATGGGGCGAGCCACAGCGGCCACCTGCTCTCGGCC  
GTCACCAACCGCAGTGATCTGGGGCCCCCTGCCAGCTCGGCCACCACGCTCGCGGACGGCGGGGAGGGGACGCA  
CGACGGCACATTCGAGCTTGCACCGTGGCTCTTCAGGCGCGGAGCAGCGCCGAGAACCGCGTCGAGATCCACA  
AGGTGGTCAGGGACCATTGGCCCTCATCTTCTCCTTCTCATCTGCTGCTGCTGCTCATGCTGCTGCTGGAAG  
TGTTTCCCAGCCAGCCTCAGGCAGCTCAGACAGTGTCTTGTACGCGAGCGCAGGAAGCAAAAGCAGAAACAGAC  
CATGCATCATAGGCTGCCATGTCTGCCAGGAATACTACGTTGATTACAACCCGAACCATGAGGGAGCGCT  
TGGTGATCATCAACGAGTATGGCTCGTGTACCTGCCACGAGCCCGCAGGGAATCGAGGTTGAGGTTCTCC  
CAGTGGCTCTCAACCCATGCGCTACCAATACGCTTGGGCAGCCGGGACGGGCGGGGACCGAGGCTGGGGT  
CTCCTGTGTCTGTCTGTATGTCCTGCTGACTGAACTTTAAGGGGATCTCTCCGAGAGACTTGACATTTT  
CTTTATTGTGTCTTAAAAACAAAGCGAATTAACACACAACAAAAACCCACCCCAACACCTTCAGGACAGTC  
TATCTTAAATTTTCATATGAGAATCTCTTCTCCCTTTGAAGATCTGTCCATATTCAGGAATCTGAGAGTGTAA  
AAAGGTGGCCATAGACAGAGAGAGAATAATCGTGCTTTGTTTTATGCTACTCTCCACCCCTGCCCATGATTA  
AACATCATGTATGTAGAAGATCTTAAGTCCATACGCAATTCATGAAGAACCTTGAAGAAAGGAATCTGCAAT  
TGGGAGCTTAAGAGCAAAATGATGACCATAGAAAGCTATGTTCTTACTTTGTGTGTGTGTCTGTATGTTTCTGCG  
TTGTGTGTCTTTGTAGGCAAGCAACGTTGTCTACACAACCGGAAATTTAGCTCACATCATTTTCATGCCCTGT  
GCCTCTAGCTTGTGAGATTTGGTGGGGGAGGTGGGGGGAACCGGAGGAATAAGGAAAGTGGTAGTTTAACT  
AAGGTTTGTGAACACTTGAATCTTTTCTTCTCAAATTAATTATCTTTAAGCTTCAAGAAACTTGCTCTGACC  
CCTCTAAGCAAACTACTAAGCATTTAAAGAGAAATCTAATTTTTAAAGGTGTAGCACCTTTTTTTTTATTCTCT  
CCACAGAGGGTGCTAATCTCATTATGCTGTGATCTGAAAGAACTTAAGGCCACAATTCACGTCTCGTCTCTG  
GGCATTTGTATGGATTGACCTCCATTGTCAGTACCTTCCAGCTGATTAAGTTTCAGCAGTGGTATTGAGGTT  
TTTCGAATATTTATATAGAAAAAAGTCTTTTTCATACGACAAATGACACTCTCACACCAAGCTTTAGCCCTAGTA  
GTTTCTTAGTTTGGACGAGGAAGCAGGTTAAATGAGACCTGTCTCTGCTGCCTCAAGAAAGCAGACATTTGGTATG  
ATTTAGCATCAACAACATTTATGAGTATATGTAAAGTAATCAGAGGGGCAATGCCACTTGTTATTCTCTCCCA  
AGTTTTCGAAGCATACACACAGATCTCTGGTAGGATTAGGGGCCACTTGTTTCCGGCTATTTTAGTCTGA  
CTTGTTCAGCAAGTTTGTAGTCCCTAGTCTATCTGACATGGCCAGTACGACAGGCGATTGATGGATCAGATGAGT  
CTGAGAAGGAACATCATCACATACCCCTCTCACAGAGAAAATTAAGAAGAACGAAATATATCTGTTTGG  
AGCAAGAGTGTATAATGTTTCAGGGTAGTCAAAATAAACATAAATTATCTCTCTAGATGAGTGGCGATGTTG  
GCTGATTTGGGTCTGCCATTGACAGAATGTCAATAAAAAAGGAATTAGCTAGAATATGACCATTAAATGTGCTT  
CTGAATAATATTTTGGATAGGTTTGAATGTCA



196/330

**FIGURE 196**

MDFLLLGLCLYWLLRRPSGVVLCLLGACFQMLPAAPSGCPQLCRCEGRLLYCEALNLTEAPH  
NLSGLLGLSLRYNSLSELRAGQFTGLMQLTWLYLDHNNHICSVQGDAFQKLRRVKELTLSSNQ  
ITQLPNTTFRPMPNLRSDLSYNKLQALAPDLFHGLRKLTLHMRANAIQFVPVRIQDCRS  
LKFLDIGYNQLKSLARNSFAGLFKLTELHLEHNDLVKVNFAHFPRILSLHSLCLRRNKVAIV  
VSSLDWVWNLEKMDLSGNEIEYMEPHVFETVPHLQSLQLDSNRLTYIEPRILNSWKSITSIT  
LAGNLWDCGRNVCALASWLSNFQGRYDGNLQCASPEYAQGEDVLDVYAFHLCEDGAEPTSG  
HLLSAVTNRSDLGPPASSATTADGGEGQHDGTFEPATVALPGGEHAENAVQIHKVVTGTMA  
LIFSFLIVVLVLYVSWKCFPASLRQLRQCFVTQRRKQKQKQTMHQMAAMSAQEYYVDYKPNH  
IEGALVIINEYGSCTCHQQPARECEV

197/330

**FIGURE 197**

GTGCAAGGAGCCGAGGCGAG**ATG**GGCGTCCTGGGCCGGGTCCCTGCTGTGGCTGCAGCTCTGC  
GCACTGACCCAGGCGGTCTCCAAACTCTGGGTCCCCAACACGGACTTCGACGTCGCAGCCAA  
CTGGAGCCAGAACCGGACCCCGTGCGCCGGCGGCCCGTTGAGTTCCCGGCGGACAAGATGG  
TGTCAGTCCTGGTGCAAGAAGGTCACGCCGTCTCAGACATGCTCCTGCCGCTGGATGGGGAA  
CTCGTCCTGGCTTCAGGAGCCGGATTTCGGCGTCTCAGACGTGGGCTCGCACCTGGACTGTGG  
CGCGGGCGAACCTGCCGTCTTCCGCGACTCTGACCGCTTCTCCTGGCATGACCCGCACCTGT  
GGCGCTCTGGGGACGAGGCACCTGGCCTCTTCTTCGTGGACGCCGAGCGCGTGCCCTGCCGC  
CACGACGACGTCTTCTTTCCGCCTAGTGCCTCCTTCCGCGTGGGGCTCGGCCCTGGCGCTAG  
CCCCGTGCGTGTCGCGAGCATCTCGGCTCTGGGCCGGACGTTACGCGCGACGAGGACCTGG  
CTGTTTTCTGCGTCCCGCGCGGGCCGCCTACGCTTCCACGGGCCGGGCGCGCT**TGA**GCGTG  
GGCCCCGAGGACTGCGCGGACCCGTGCGGCTGCGTCTGCGGCAACGCGGAGGCGCAGCCGTG  
GATCTGCGCGGCCCTGCTCCAGCCCCCT

198/330

**FIGURE 198**

MGVLGRVLLWLQLCALTQAVSKLWVPNTDFDVAANWSQNRTPCAGGAVEFPADKMVSVLVQE  
GHAVSDMLLPLDGELVLASGAGFGVSDVGSHLDCGAGEPAVFRDSDRFSWHDPHLWRSGDEA  
PGLFFVDAERVPCRHDDVFFPPSASFRVGLGPGASPVRVRSISALGRTFTRDEDLAVFLASR  
AGRLRFHGPGALSVGPEDCADPSGCVCGNAEAQPWICAALLQP

### FIGURE 199

[illegible]

200/330

**FIGURE 200**

MGPVKQLKRMFEPTRLIATIMVLLCFALTLCSAFWWHNKGLALIFCILQSLALTWYSLSFIP  
FARDAVKKCFVCLA

201/330

**FIGURE 201**

TTGAGCGCAGGTGAGCTCCTGCGCGTTCCGGGGGCGTTCCCTCCAGTCACCCCTCCCGCCGTTACCCGCGGGCGCGC  
CCGAGGGAGTCTCCTCCAGACCCCTCCCTCCCGTTGCTCCAACTAATACGGACTGAACGGATCGCTGCGAGGGT  
GGGAGAGAAAATTAGGGGGAGAAAGGACAGAGAGAGCAACTACCATCCATAGCCAGATAGATTATCTTACACTG  
AACTGATCAAGTACTTTGAAAATGACTTCGAAATTTATCTTGGTGTCTTCATACTTGCTGCACTGAGTCTTTC  
AACCACCTTTTCTCTCCAAGTACAGCAGCAAAAGGTTCTACTAGTTTCTTTTGATGGATTCCGTTGGGATTACT  
TATATAAAGTTCCAACGCCCCATTTTCATTATATTATGAAATATGGTGTTCACGTGAAGCAAGTTACTAATGTT  
TTTATTACAAAAACCTACCCTAACCATTTATCTTTGGTAACTGGCCTCTTTCAGAGAAATCATGGGATTGTTGC  
AAATGATATGTTTGATCCTATTTCGGAACAAATCTTCTCCTTGGATCACATGAATATTTATGATTCCAAGTTTT  
GGGAAGAAGCGACACCAATATGGATCACAAACCAGAGGGCAGGACATACTAGTGGTGCAGCCATGTGGCCCCGA  
ACAGATGTAAAAATACATAAGCGCTTTCCTACTCATTACATGCCTTACAATGAGTCAGTTTCATTTGAAGATAG  
AGTTGCCAAAATTGTTGAATGGTTTACGTCAAAAGAGCCCATAAATCTTGGTCTTCTCTATTGGGAAGACCCTG  
ATGACATGGGCCACCATTTGGGACCTGACAGTCCGCTCATGGGGCCTGTCAATTCAGATATTGACAAGAAGTTA  
GGATATCTCATACAAATGCTGAAAAAGGCAAGTTGTGGAACACTCTGAACCTAATCATCACAAGTGATCATGG  
AATGACGCAGTGCTCTGAGGAAAGGTTAATAGAACTTGACCAGTACCTGGATAAAGACCCTATACCCCTGATTG  
ATCAATCTCCAGTAGCAGCCATCTTGCCAAAAGAAGGTAAATTTGATGAAGTCTATGAAGCACTAACTCACGCT  
CATCCTAATCTTACTGTTTACAAAAAAGAAGACGTTCCAGAAAGGTGGCATTACAAATACAACAGTCGAATTCA  
ACCAATCATAGCAGTGGCTGATGAAGGGTGGCACATTTTACAGAATAAGTCAGATGACTTTCTGTTAGGCAACC  
ACGGTTACGATAATGCGTTAGCAGATATGCATCCAATATTTTTAGCCCATGGTCTTGCCTTCAGAAAGAATTTT  
TCAAAAGAAGCCATGAACCTCCACAGATTTGTACCCACTACTATGCCACCTCCTCAATATCACTGCCATGCCACA  
CAATGGATCATTTCTGGAATGTCCAGGATCTGCTCAATTCAGCAATGCCAAGGGTGGTCCCTTATACACAGAGTA  
CTATACTCCTCCCTGGTAGTGTTAAACCAGCAGAATATGACCAAGAGGGGTCAATCCCTTATTTCATAGGGGTC  
TCTCTTGGCAGCATTATAGTGATTGTATTTTTTGTAAATTTTCATTAAGCATTAAATTCACAGTCAAATACCTGC  
CTTACAAGATATGCATGCTGAAATAGCTCAACCATTATTACAAGCCTAATGTTACTTTGAAGTGGATTTGCATA  
TTGAAGTGGAGATTCCATAATTATGTCAGTGTTTTAAAGGTTTTCAAATTTCTGGGAAACCAGTTCCAAACATCTGC  
AGAAACCATTAAGCAGTTACATATTTAGGTATACACACACACACACACACATACACACACACGGACCAAA  
ATACTTACACCTGCAAAGGAATAAAGATGTGAGAGTATGTCTCCATTGTTCACTGTAGCATAGGGATAGATAAG  
ATCCTGCTTTATTTGGACTTGGCGCAGATAATGTATATATTTAGCAACTTTGCACTATGTAAAGTACCTTATAT  
ATTGCACTTTAAATTTCTCTCCTGATGGGTACTTTAATTTGAAATGCACCTTATGGACAGTTATGTCTTATAAC  
TTGATTGAAAATGACAACCTTTTTGCACCCATGTCACAGAATACTTGTTACGCATTGTTCAAACCTGAAGGAAATT  
TCTAATAATCCCGAATAATGAACATAGAAATCTATCTCCATAAATTGAGAGAAGAAGAAGGTGATAAGTGTTGA  
AAATTAATGTGATAACCTTTGAACCTTGAATTTTGGAGATGTATTCCCAACAGCAGAATGCAACTGTGGGCAT  
TTCTTGTCTTATTTCTTTCCAGAGAACGTGGTTTTTCATTTATTTTTCCCTCAAAAGAGAGTCAAATACTGACAG  
ATTCGTTCTAAATATATTGTTTCTGTCAAAAATTATTTGTGATTTCTGATGAGTCATATTACTGTGATTTTCA  
TAATAATGAAGACACCATGAATATACTTTTCTCTATATAGTTTCAGCAATGGCCTGAATAGAAGCAACCAGGCA  
CCATCTCAGCAATGTTTTCTCTTGTGTTGTAATTATTTGCTCCTTTGAAATTAATCACTATTAATTACATTAA  
AAATCAAATTGGATAAAAAAAAAAAAAAAAAAAAAA

202/330

**FIGURE 202**

MTSKFILVSFILAALSSTTFSLQLDQQKVLLVSFDGFRWDYLYKVPTPHFHYIMKYGVHVK  
QVTNVFITKTYPNHYTLVTGLFAENHGIVANDMFDPIRNKSFSLDHMNIYDSKFWEEATPIW  
ITNQ RAGHTSGAAMWPGTDVKIHKRFPTHYMPYNESVSFEDRVAKIVEWFTSKEPINLGLLY  
WEDPDDMGHHLGPDSPLMGPVISDIDKKLGYLIQMLKKAKLWNTLNLIITSDHGMTQCSEER  
LIELDQYLDKDHYTELIDQSPVAAILPKEGKFDEVYEALTHAHPNLTVYKKEDVPERWHYKYN  
SRIQPIIAVADEGWHILQNKSDDFLLGNHGYDNALADMHPIFLAHGPAFRKNFSKEAMNSTD  
LYPLLCHLLNITAMPHNGSFWNVQDLLNSAMPRVVPYTQSTILLPGSVKPAEYDQEGSYPYF  
IGVSLGSIIVIVFFVIFIKHLIHSQIPALQDMHAEIAQPLLQA

**Signal Peptide:**

amino acids 1-22

**Transmembrane Domain:**

amino acids 429-452

**N-glycosylation sites:**amino acids 101-104, 158-161, 292-295, 329-332, 362-365, 369-  
372, 382-385, 389-392**Somatomedin B Domain:**

amino acids 69-85

**Sulfatase protein Region:**

amino acids 212-241

203/330

**FIGURE 203**

GGATTTTTGTGATCCGCGATTTCGCTCCACGGGCGGGACCTTTGTAAGTGCAGGGAGGCCAG  
GACAGGCCCCACCCTGCGGGGCGGGAGGCAGCCGGGGTGAGGGAGGTGAAGAAACCAAGACGC  
AGAGAGGCCAAGCCCCCTTGCCCTGGGTCACACAGCCAAAGGAGGCAGAGCCAGAACTCACAA  
CCAGATCCAGAGGCAACAGGGAC**ATG**GCACCTGGGACGAAAAGGCAGTCACCCGCAGGGCC  
AAGGTGGCTCCCGCTGAGAGGATGAGCAAGTTCTTAAGGCACTTCACGGTCGTGGGAGACGA  
CTACCATGCCTGGAACATCAACTACAAGAAATGGGAGAATGAAGAGGAGGAGGAGGAGGAGG  
AGCAGCCACCACCCACACCAGTCTCAGGCGAGGAAGGCAGAGCTGCAGCCCCCTGACGTTGCC  
CCTGCCCCCTGGCCCCGCACCCAGGGCCCCCCTTGACTTCAGGGGCATGTTGAGGAACTGTT  
CAGCTCCCACAGGTTTCAGGTCATCATCATCTGCTTGGTGGTTCTGGATGCCCTCCTGGTGC  
TTGCTGAGCTCATCCTGGACCTGAAGATCATCCAGCCCGACAAGAATAACTATGCTGCCATG  
GTATTCCACTACATGAGCATCACCATCTTGGTCTTTTTTATGATGGAGATCATCTTTAAATT  
ATTTGTCTTCCGCCTGAGTTCTTTCACCACAAGTTTGAGATCCTGGATGCCCGTCGTGGTGG  
TGGTCTCATTCATCCTGGACATTGTCCTCCTGTTCCAGGAGCACCAGTTTGAGGCTCTGGGC  
CTGCTGATTCTGCTCCGGCTGTGGCGGGTGGCCCGGATCATCAATGGGATTATCATCTCAGT  
TAAGACACGTTTCAAGACGGCAACTCTTAAGGTTAAAACAGATGAATGTACAATTGGCCGCCA  
AGATTCAACACCTTGAGTTCAGCTGCTCTGAGAAGCCCCCTGGACT**TGA**TGAGTTTGCTGTATC  
AACCTGTAAGGAGAAGCTCTCTCCGGATGGCTATGGGAATGAAAGAATCCGACTTCTACTCT  
CACACAGCCACCGTGAAAGTCTTGGAGTAAAATGTGCTGTGTACAGAAGAGAGAGAAGGAAG  
CAGGCTGGCATGTTCACTGGGCTGGTGTACGACAGAGAACCTGACAGTCACTGGCCAGTTA  
TCACTTCAGATTACAAATCACACAGAGCATCTGCCTGTTTTCAATCACAAGAGAACAAAACC  
AAAATCTATAAAGATATTCTGAAAATATGACAGAATTTGACAAATAAAAGCATAAACGTGTA  
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA



204/330

**FIGURE 204**

MATWDEKAVTRRAKVAPAERMSKFLRHFTVVGDDYHAWNINYYKKWENEEEEEEEEEQPPPTPV  
SGEEGRAAAPDVAPAPGPAPRAPLDFRGMLRKLFSSSHRFQVIIICLVVLDALLVLAELILD  
KIIQPDKNNYAAMVFHYMSITILVFFMMEIIFKLFVFRLLSSFTTSLRSWMPVVVVVSFILD  
VLLFQEHQFEALGLLILLRLWRVARIINGIIISVKTRSERQLRLKQMNVQLAAKIQHLEFS  
CSEKPLD

205/330

**FIGURE 205**

CGGCTCGAGCTCGAGCCGAATCGGCTCGAGGGGCGAGTGGAGCACCCAGCAGGCCGCCAAC**AT**  
**G**CTCTGTCTGTGCCTGTACGTGCCGGTCATCGGGGAAGCCCAGACCGAGTTCCAGTACTTTG  
AGTCGAAGGGGCTCCCTGCCGAGCTGAAGTCCATTTTCAAGCTCAGTGTCTTCATCCCCCTCC  
CAGGAATTCTCCACCTACCGCCAGTGGGAAGCAGAAAATTGTACAAGCTGGAGATAAGGACCT  
TGATGGGCAGCTAGACTTTGAAGAATTTGTCCATTATCTCCAAGATCATGAGAAGAAGCTGA  
GGCTGGTGTTTAAGATTTTGGACAAAAAGAATGATGGACGCATTGACGCGCAGGAGATCATG  
CAGTCCCTGCGGGACTTGGGAGTCAAGATATCTGAACAGCAGGCAGAAAAAATTCTCAAGAG  
CATGGATAAAAAACGGCACGATGACCATCGACTGGAACGAGTGGAGAGACTACCACCTCCTCC  
ACCCCGTGGAAAACATCCCCGAGATCATCTCTACTGGAAGCATTCACGATCTTTGATGTG  
GGTGAGAATCTAACGGTCCCGGATGAGTTACAGTGGAGGAGAGGCAGACGGGGATGTGGTG  
GAGACACCTGGTGGCAGGAGGTGGGGCAGGGGCCGTATCCAGAACCTGCACGGCCCCCTGG  
ACAGGCTCAAGGTGCTCATGCAGGTCCATGCCTCCCGCAGCAACAACATGGGCATCGTTGGT  
GGCTTCACTCAGATGATTCGAGAAGGAGGGGCCAGGTCACTCTGGCGGGGCAATGGCATCAA  
CGTCTCAAATTTGCCCCGAATCAGCCATCAAATTCATGGCCTATGAGCAGATCAAGCGCC  
TTGTTGGTAGTGACCCAGGAGACTCTGAGGATTCACGAGAGGCTTGTGGCAGGGTCTTGGCA  
GGGGCCATCGCCCAGAGCAGCATCTACCCAATGGAGGTCTGAAGACCCGGATGGCGCTGCG  
GAAGACAGGCCAGTACTCAGGAATGCTGGACTGCGCCAGGAGGATCCTGGCCAGAGAGGGGG  
TGGCCGCCTTCTACAAAGGCTATGTCCCCAACATGTCTGGGCATCATCCCCTATGCCGGCATC  
GACCTTGCAGTCTACGAGACGCTCAAGAATGCCTGGCTGCAGCACTATGCAGTGAACAGCGC  
GGACCCCGCGTGTGTGTGCTCCTGGCCTGTGGCACCATGTCCAGTACCTGTGGCCAGCTGG  
CCAGCTACCCCTGGCCCTAGTCAGGACCCGGATGCAGGCGCAAGCCTCTATTGAGGGCGCT  
CCGGAGGTGACCATGAGCAGCCTCTTCAAACATATCCTGCGGACCGAGGGGGCCTTCGGGCT  
GTACAGGGGGCTGGCCCCCACTTCATGAAGGTCACTCCAGCTGTGAGCATCAGCTACGTGG  
TCTACGAGAACCTGAAGATCACCTTGGGCGTGCAGTCCGCG**TGAC**GGGGGGAGGGCCGCCCG  
GCAGTGGACTCGCTGATCCTGGGCCGAGCCTGGGGTGTGCAGCCATCTCATTTCTGTGAATG  
TGCCAACACTAAGCTGTCTCGAGCCAAGCTGTGAAAACCTTAGACGCACCCGCAGGGAGGGT  
GGGGAGAGCTGGCAGGCCCAGGGCTTGTCTGCTGACCCAGCAGACCCTCCTGTTGGTTCC  
AGCGAAGACCACAGGCATTCCTTAGGGTCCAGGGTCAGCAGGCTCCGGGCTCACATGTGTAA  
GGACAGGACATTTTCTGCAGTGCCTGCCAATAGTGAGCTTGGAGCCTGGAGGCCGGCTTAGT  
TCTTCCATTTACCCCTTGCAGCCAGCTGTTGGCCACGGCCCTGCCCTCTGGTCTGCCGTGC  
ATCTCCCTGTGCCCTCTTGCTGCCTGCCTGTCTGCTGAGGTAAGGTGGGAGGAGGGCTACAG  
CCCACATCCCACCCCTCGTCCAATCCCATAATCCATGATGAAAGGTGAGGTCACGTGGCCT  
CCCAGGCCTGACTTCCAACCTACAGCATTGACGCCAACTTGGCTGTGAAGGAAGAGGAAAG  
GATCTGGCCTTGTGGTCACTGGCATCTGAGCCCTGCTGATGGCTGGGGCTCTCGGGCATGTCT  
TGGGAGTGCAGGGGCTCGGGCTGCCTGGCTGGCTGCACAGAAGGCAGTGTGGGGCTCA  
TGGTGTCTCTGAGCTGGCCTGGACCCTGTGAGGATGGGCCCCACCTCAGAACCAAACCTCACTG  
TCCCCACTGTGGCATGAGGGCAGTGGAGCACCATGTTTGAGGGCGAAGGGCAGAGCGTTTGT  
GTGTTCTGGGGAGGGAAGGAAAAGGTGTTGGAGGCCCTTAATTATGGACTGTTGGGAAAAGGG  
TTTTGTCCAGAAGGACAAGCCGGACAAATGAGCGACTTCTGTGCTTCCAGAGGAAGACGAGG  
GAGCAGGAGCTTGGCTGACTGCTCAGAGTCTGTTCTGACGCCCTGGGGGTTCTGTGCCAACC  
CCAGCAGGGGCGCAGCGGGACCGCCACATTCCACTTGTGTCACTGCTTGGAACTATTT  
ATTTTGTATTTATTTGAACAGAGTTATGTCTAACTATTTTTATAGATTTGTTTAAATTAATA  
GCTTGTCATTTTCAAGTTCATTTTTTATTCATATTTATGTTTCATGGTTGATTGTACCTTCCC  
AAGCCCGCCAGTGGGATGGGAGGAGGAGGAGAAGGGGGCCTTGGGCCGCTGCAGTCACAT  
CTGTCCAGAGAAATTCCTTTTGGGACTGGAGGCAGAAAAGCGGCCAGAAAGGCAGCAGCCCTG  
GCTCCTTTCTTTTGGCAGGTTGGGGAAGGGCTTGGCCCCAGCCTTAGGATTTAGGGTTTGA  
CTGGGGGCGTGGAGAGAGAGGGGAGGAACCTCAATAACCTTGAAGGTGGAATCCAGTTATTTCT  
CTGCGCTGCGAGGGTTTCTTTATTTCACTCTTTTCTGAATGTCAAGGCAGTGAGGTGCCTCT  
CACTGTGAATTTGTGGTGGGCGGGGCTGGAGGAGAGGGTGGGGGCTGGCTCCGCTCCCTCC  
CAGCCTTCTGCTGCCCTTGTAAACAATGCCGGCCAACCTGGCGACCTCACGGTGTCACTTCC  
ATTCCACCAGAATGACCTGATGAGGAAATCTTCAATAGGATGCAAAGATCAATGCAAAAATT  
GTTATATATGAACATATAACTGGAGTCGTCAAAAAGCAAATTAAGAAAGAATTGGACGTTAG  
AAGTTGTCATTTAAAGCAGCCTTCTAATAAAGTTGTTTCAAAGCTGAAAAA  
AA

206/330

**FIGURE 206**

MLCLCLYVPVIGEAQTEFQYFESKGLPAELKSIFKLSVFIPSQEFSTYRQWKQKIVQAGDKD  
LDGQLDFEEFVHYLQDHEKKLRLVFKILDKKNDGRIDAQEIMQSLRDLGVKISEQQAEEKILK  
SMDKNGTMTIDWNEWRDYHLLHPVENIPEIILYWKHSTIFDVGENLTPDEFTVEERQTMW  
WRHLVAGGGAGAVSRTCTAPLDRLKVLMOVHASRSNNMGIVGGFTQMIREGGARSLWRGNGI  
NVLKIAPESAIFMAYEQIKRLVGSDQETLRIHERLVAGSLAGAIQSSIYPMEVLKTRMAL  
RKTGQYSGMLDCARRILAREGVAAFYKGYVPNMLGIIIPYAGIDLAVYETLKNWLQHYAVNS  
ADPGVFVLLACGTMSSTCGQLASYPLALVRTRMQAQASIEGAPEVTMSSLFKHILRTEGAFG  
LYRGLAPNFMKVIPAVSISYVVYENLKITLGVQSR

**Important features:****Signal peptide:**

amino acids 1-16

**Transmembrane domain:**

amino acids 284-304, 339-360, 376-394

**Mitochondrial energy transfer proteins signature.**

amino acids 206-215, 300-309

**N-glycosylation site.**

amino acids 129-133, 169-173

**Elongation Factor-hand calcium-binding protein.**

amino acids 54-73, 85-104, 121-140



208/330

**FIGURE 208**

MASLGQILFWSIISIIIIILAGAIALIIGFGISGRHSITVTTVASAGNIGEDGILSCTFEPDI  
KLSDIVIQWLKEGVLGLVHEFKEGKDELSEQDEMFRGRTAVFADQVIVGNASLRLKNVQLTD  
AGTYKCYIIITSKGKGNNANLEYKTGAFSMPEVNVDYNASSETLRCEAPRWFPQPTVVWASQVD  
QGANFSEVSNTSFELNSENVTMKVSVLYNVTINNTYSCMIENDIAKATGDIKVTESEIKRR  
SHLQLLNSKASLCVSSFFAISWALLPLSPYLMLK

209/330

**FIGURE 209**

[illegible]

210/330

**FIGURE 210**

MAASLGQVLALVLVAALWGGTQPLLKRASAGLQRVHEPTWAQQLQEMKTLFLNTEYLMFPL  
LNQCGSLLYYLTLASTDLTLAVPICNSLAIIFTLIVGKALGEDIGGKRKLDYCECGTQLCGS  
RHTCVSSFPEPISPEWVRTRPFPILPFPLQLFCFLVAIRVPFPWTVWRKTEAGVWD

211/330

**FIGURE 211**

CTTCTGTAGGACAGTCACCAGGCCAGATCCAGAAGCCTCTCTAGGCTCCAGCTTTCTCTGTG  
GAAGATGACAGCAATTATAGCAGGACCCTGCCAGGCTGTGCGAAAAGATTCCGCAATAAACT  
TTGCCAGTGGGAAGTACCTAGTGAAACGGCCTAAGATGCCACTTCTTCTCATGTCCCAGGCT  
TGAGGCCCTGTGGTCCCCATCCTTGGGAGAAGTCAGCTCCAGCACCATGAAGGGGCATCCTCG  
TTGCTGGTATCACTGCAGTGCTTGTTGCAGCTGTAGAATCTCTGAGCTGCGTGCAGTGTAAT  
TCATGGGAAAAATCCTGTGTCAACAGCATTGCCTCTGAATGTCCCTCACATGCCAACACCAG  
CTGTATCAGCTCCTCAGCCAGCTCCTCTCTAGAGACACCAGTCAGATTATACCAGAATATGT  
TCTGCTCAGCGGAGAACTGCAGTGAGGAGACACACATTACAGCCTTCACTGTCCACGTGTCT  
GCTGAAGAACACTTTTCATTTTGTAAAGCCAGTGCTGCCAAGGAAAGGAATGCAGCAACACCAG  
CGATGCCCTGGACCCTCCCCTGAAGAACGTGTCCAGCAACGCAGAGTGCCCTGCTTGTTATG  
AATCTAATGGAACCTCCTGTCTGTTGGGAAGCCCTGGAAATGCTATGAAGAAGAACAGTGTGTC  
TTTCTAGTTGCAGAACTTAAGAATGACATTGAGTCTAAGAGTCTCGTGCTGAAAGGCTGTTC  
CAACGTCAGTAACGCCACCTGTCAGTTCCTGTCTGGTGAAAACAAGACTCTTGAGGAGTCA  
TCTTTCGAAAGTTTGAGTGTGCAAATGTAAACAGCTTAACCCCCACGTCTGCACCAACCACT  
TCCCACAACGTGGGCTCCAAAGCTTCCCTCTACCTCTTGGCCCTTGCCAGCCTCCTTCTTCG  
GGGACTGCTGCCCCTGAAGGTCCTGGGGCTGCACTTTGCCCAGCACCCCATTTCTGCTTCTCTG  
AGGTCCAGAGCACCCCCTGCGGTGCTGACACCCTCTTCCCTGCTCTGCCCCGTTTAACTGC  
CCAGTAAGTGGGAGTCACAGGTCTCCAGGCAATGCCGACAGCTGCCTTGTTCTTCATTATTA  
AAGCACTGGTTCATTCACTGCCAAAAAAAAAAAAAAAAAAAAAAAAAAAAA



212/330

**FIGURE 212**

MKGILVAGITAVLVAAVESLSCVQCNSWEKSCVNSIASECPSHANTSCISSSASSSLETPVR  
LYQNMFCSAENCSEETHITAFTVHVSAEEHFHFVSQCCQGKECSNTSDALDPPLKNVSSNAE  
CPACYESNGTSCRGKPWKCYEEEQCVFLVAELKNDIESKSLVLKGCSNVSNATCQFLSGENK  
TLGGVIFRKFEKANVNSLTPTSAPTTSHNVGSKASLYLLALASLLLRGLLP

213/330

**FIGURE 213**

GGCCTCGGTTCAAACGACCCGGTGGGTCTACAGCGGAAGGGAGGGAGCGAAGGTAGGAGGCA  
GGGCTTGCCTCACTGGCCACCCTCCCAACCCCAAGAGCCCAGCCCC**ATG**GTCCCCGCCGCCG  
GCGCGCTGCTGTGGGTCTGCTGCTGAATCTGGGTCCCCGGGCGGCGGGGGCCCAAGGCCTG  
ACCCAGACTCCGACCGAAATGCAGCGGGTCAGTTTACGCTTTGGGGGCCCCATGACCCGCAG  
CTACCGGAGCACCGCCCGGACTGGTCTTCCCCGGAAGACAAGGATAATCCTAGAGGACGAGA  
ATGATGCCATGGCCGACGCCGACCGCCTGGCTGGACCAGCGGCTGCCGAGCTCTTGGCCGCC  
ACGGTGTCCACCGGCTTTAGCCGGTTCGTCGCCATTAACGAGGAGGATGGGTCTTCAGAAGA  
GGGGGTGTGATTAATGCCGGAAGGATAGCACCAGCAGAGAGCTTCCCAGTGCGACTCCCA  
ATACAGCGGGGAGTTCCAGCACGAGGTTTATAGCCAATAGTCAGGAGCCTGAAATCAGGCTG  
ACTTCAAGCCTGCCGCGCTCCCCCGGGAGGTCTACTGAGGACCTGCCAGGCTCGCAGGCCAC  
CCTGAGCCAGTGGTCCACACCTGGGTCTACCCCGAGCCGGTGGCCGTCACCCTCACCCACAG  
CCATGCCATCTCCTGAGGATCTGCGGCTGGTGCTGATGCCCTGGGGCCCGTGGCACTGCCAC  
TGCAAGTCGGGCACCATGAGCCGGAGCCGGTCTGGGAAGCTGCACGGCCTTTCCGGGCGCCT  
TCGAGTTGGGGCGCTGAGCCAGCTCCGCACGGAGCACAAGCCTTGACCTATCAACAATGTC  
CCTGCAACCGACTTCGGGAAGAGTGCCCCCTGGACACAAGTCTCTGTACTGACACCAACTGT  
GCCTCTCAGAGCACCAACAGTACCAGGACCACCACTACCCCTTCCCCACCATCCACCTCAG  
AAGCAGTCCCAGCCTGCCACCCGCCAGCCCCTGCCAGCCCTGGCTTTTTTGGAACGGGTCA  
GGATTGGCCTGGAGGATATTTGGAATAGCCTCTCTTCAGTGTTACAGAGATGCAACCAATA  
GACAGAAACCAGAGG**TAA**TGGCCACTTCATCCACATGAGGAGATGTCAGTATCTCAACCTCT  
CTTGCCCTTTCAATCCTAGCACCCACTAGATATTTTGTAGTACAGAAAAACAAAACCTGGAAAA  
CACAA

214/330

**FIGURE 214**

MVPAAGALLWVLLLNLGPRAGAQLTQTPTEMQRVSLRFGGPMTRSYRSTARTGLPRKTRI  
ILEDENDAMADADRLAGPAAELLAATVSTGFSRSSAINEEDGSSEEGVVINAGKDSTSREL  
PSATPNTAGSSSTRFIANSQEPEIRLTSSLPRSPGRSTEDLPGSQATLSQWSTPGSTPSRWP  
SPSPTAMPSPEDLRLVLMWPWGPWHCHCKSGTMSRSRSGKLHGLSGRLRVGALSQLRTEHKPC  
TYQQPCPNRLREECPLDTSLCDTNCASQSTTSTRTTTTPTIHLRSSPSLPPASPCPALA  
FWKRVRIGLEDIWNSLSSVFTEMQPIDRNQR

215/330

**FIGURE 215**

CCCGGGTCGACCCACGCGTCCGGGGAGAAAGGATGGCCGGCCTGGCGGCGCGGTTGGTCCTGCTAGCTGGGGCA  
GCGGCGCTGGCGAGCGGCTCCCAGGGCGACCGTGAGCCGGTGTACCGCGACTGCGTACTGCAGTGCGAAGAGCA  
GAACTGCTCTGGGGGCGCTCTGAATCACTTCCGCTCCCGCCAGCCAATCTACATGAGTCTAGCAGGCTGGACCT  
GTCGGGACGACTGTAAGTATGAGTGTATGTGGGTACCGTTGGGCTCTACCTCCAGGAAGGTCACAAAGTGCCCT  
CAGTTCATGGCAAGTGCCCTTCTCCCGGTTCTGTTCTTTCAAGAGCCGGCATCGGCGCTGGCCTCGTTTCT  
CAATGGCCTGGCCAGCCTGGTGATGCTCTGCCGCTACCGCACCTTCGTGCCAGCCTCCTCCCCATGTACCACA  
CCTGTGTGGCCTTCGCCTGGGTGTCCCTCAATGCATGGTTCTGGTCCACAGTCTTCCACACCAGGGACACTGAC  
CTCACAGAGAAAATGGACTACTTCTGTGCCTCCACTGTCATCCTACACTCAATCTACCTGTGCTGCGTCAGGAC  
CGTGGGGCTGCAGCACCCAGCTGTGGTCAGTGCCTTCCGGGCTCTCCTGCTGCTCATGCTGACCGTGACAGTCT  
CCTACCTGAGCCTCATCCGCTTCGACTATGGCTACAACCTGGTGGCCAACGTGGCTATTGGCCTGGTCAACGTG  
GTGTGGTGGCTGGCCTGGTGCTGTGGAACCAGCGCGGCTGCCTCACGTGCGCAAGTGCGTGGTGGTGGTCTT  
GCTGCTGCAGGGGCTGTCCCTGCTCGAGCTGCTTGACTTCCCACCGCTCTTCTGGGTCTGGATGCCCATGCCA  
TCTGGCACATCAGCACCATCCCTGTCCACGTCTCTTTTTTCAGCTTTCTGGAAGATGACAGCCTGTACCTGCTG  
AAGGAATCAGAGGACAAGTTCAAGCTGGACTGAAGACCTTGGAGCGAGTCTGCCCCAGTGGGGATCCTGCCCC  
GCCCTGCTGGCCTCCCTTCTCCCCCTCAACCTTGAGATGATTTTCTCTTTTCAACTTCTTGAACCTGGACATGA  
AGGATGTGGGCCCAGAATCATGTGGCCAGCCACCCCTGTTGGCCCTCACCAGCCTTGAGTCTGTTCTAGGG  
AAGCCCTCCAGCATCTGGGACTCGAGAGTGGGCAGCCCTCTACCTCCTGGAGCTGAACTGGGGTGGAACTGA  
GTGTGTTCTTAGCTCTACCGGGAGGACAGCTGCCTGTTTCTCCCCACCAGCCTCCTCCCCACATCCCCAGCTG  
CCTGGCTGGGTCTGAAGCCCTCTGTCTACCTGGGAGACCAGGGACCACAGGCCTTAGGGATACAGGGGGTCCC  
CTTCTGTACCACCCCCACCCCTCCTCCAGGACACCACTAGGTGGTGTGCTGGATGCTTGTCTTTGGCCAGCCAA  
GGTTCACGGCGATTCTCCCCATGGGATCTTGAGGGACCAAGCTGCTGGGATTGGGAAGGAGTTTACCCTGACC  
GTTGCCCTAGCCAGGTTCCAGGAGGCCTCACCATACTCCCTTTCAGGGCCAGGGCTCCAGCAAGCCAGGGCA  
AGGATCCTGTGCTGCTGTCTGGTTGAGAGCCTGCCACCGTGTGTGCGGAGTGTGGGCCAGGCTGAGTGCATAGG  
TGACAGGGCCGTGAGCATGGGCCTGGGTGTGTGTGAGCTCAGGCCTAGGTGCGCAGTGTGGAGACGGGTGTTGT  
CGGGGAAGAGGTGTGGCTTCAAAGTGTGTGTGTGCAGGGGGTGGGTGTGTTAGCGTGGGTAGGGGAACGTGTG  
TGCGCGTGTGGTGGGCATGTGAGATGAGTGACTGCCGGTGAATGTGTCCACAGTTGAGAGGTTGGAGCAGGAT  
GAGGGAATCCTGTACCATCAATAATCACTTGTGGAGCGCCAGCTCTGCCCAAGACGCCACCTGGGCGGACAGC  
CAGGAGCTCTCCATGGCCAGGCTGCCTGTGTGCATGTTCCCTGTCTGGTGCCCTTTGCCCGCTCCTGCAAAC  
CTCACAGGGTCCCCACACAACAGTGCCCTCCAGAAGCAGCCCTCGGAGGCAGAGGAAGGAAAATGGGGATGGC  
TGGGGCTCTCTCCATCCTCCTTTTCTCCTTGCCCTTCGCATGGCTGGCCTTCCCCTCCAAAACCTCCATTCCCCT  
GCTGCCAGCCCCTTTGCCATAGCCTGATTTTGGGGAGGAGGAAGGGGCGATTTGAGGGAGAAGGGGAGAAAGCT  
TATGGCTGGGTCTGGTTTCTTCCCTTCCCAGAGGGTCTTACTGTTCCAGGGTGGCCCCAGGGCAGGCAGGGGCC  
ACACTATGCTGTGCCCTGGTAAAGGTGACCCCTGCCATTTACCAGCAGCCCTGGCATGTTCCCTGCCCCACAGG  
AATAGAATGGAGGGAGCTCCAGAACTTTCCATCCCAAAGGCAGTCTCCGTGGTTGAAGCAGACTGGATTTTGTG  
CTCTGCCCCTGACCCCTTGTCCCTCTTTGAGGGAGGGGAGCTATGCTAGGACTCCAACCTCAGGGACTCGGGTG  
GCCTGCGCTAGCTTCTTTTGATACTGAAAACTTTAAAGGTGGGAGGGTGGCAAGGGATGTGCTTAATAAATCAA  
TTCCAAGCCTCAAAAAAAAAAAAAAAAAA

216/330

**FIGURE 216**

MAGLAARLVLLAGAAALASGSQGDREPVYRDCVLQCEEQNCSGGALNHFRSRQPIYMSLAGW  
TCRDDCKYECMWVTVGLYLQEGHKVPQFHGKWPFSSRFLFFQEPASAVASFLNGLASLVMLCR  
YRTFVPASSPMYHTCVAFAWVSLNAWFWSTVFHTRDSDLTEKMDYFCASTVILHSIYLCCVR  
TVGLQHPAVVSAFRALLLLMLTVHVSYSLSLIRFDYGYNLVANVAIGLVNVVWWLAWCLWNQR  
RLPHVRKCVVVVLLQGLSLLELLDFPPLFWVLDAAHAIWHISTIPVHVLFFSFLEDDSLYLL  
KESEDKFKLD

**Important features:****Signal peptide:**

amino acids 1-20

**Transmembrane domains:**

amino acids 105-123, 138-156, 169-185, 193-209, 221-240, 256-272

**N-glycosylation site.**

amino acids 40-44

**N-myristoylation site.**

amino acids 43-49

**CUB domain proteins profile.**

amino acids 285-302

**Amiloride-sensitive sodium channels proteins.**

amino acids 162-186

217/330

**FIGURE 217**

[illegible]

218/330

**FIGURE 218**

MAPQSLPSSRMAPLGMLLGLLMAACFTFCLSHQNLKEFALTNPEKSSTKETERKETKAEEEL  
DAEVLEVVFHPTHEWQALQPGQAVPAGSHVRLNLQTGEREAKLQYEDKFRNNLKGKRLDINTN  
TYTSQDLKSALAKFKEGAEMESSKEDKARQAEVKRLFRPIEELKKDFDELNVVIETDMQIMV  
RLINKFNSSSSSLEEKIAALFDLEYVYVHQMDNAQDLLSFGGLQVVINGLNSTEPLVKEYAAF  
VLGAAFSSNPKVQVEAIEGGALQKLLVILATEQPLTAKKKVLFALCSLLRHFPYAQRQFLKL  
GGLQVLRTLVQEKGTEVLAVRVVTLLYDLVTEKMFEEEEAELTQEMSPEKLQQYRQVHLLPG  
LWEQGWCEITAHLLALPEHDAREKVLQTLGVLLTTCRDRYRQDPQLGRTLASLQAEYQVLAS  
LELQDGEDEGYFQELLGSVNSLLKELR

**Important features:****Signal peptide:**

amino acids 1-29

**Hypothetical YJL126w/YLR351c/yhcX family protein.**

amino acids 364-373

**N-glycosylation site.**

amino acids 193-197, 236-240

**N-myristoylation site.**

amino acids 15-21, 19-25, 234-240, 251-257, 402-408, 451-457

**Homologous region SLS1 protein.**

amino acids 68-340

219/330

**FIGURE 219**

TTCGGCTTCCGTAGAGGAAGTGGCGCGGACCTTCATTTGGGGTTTCGGTTCCCCCCTTCCC  
CTTCCCCGGGGTCTGGGGGTGACATTGCACCGCGCCCCCTCGTGGGGTTCGCGTTGCCACCCCA  
CGCGGACTCCCCAGCTGGCGCGCCCCCTCCCATTTGCCTGTCTGGTCAGGCCCCCACCCTTCC  
TCCCACCTGACCAGCC**ATG**GGGGCTGCGGTGTTTTTCGGCTGCACTTTCGTCGCGTTTCGGC  
CCGGCCTTCGCGCTTTTCTTGATCACTGTGGCTGGGGACCCGCTTCGCGTTATCATCCTGGT  
CGCAGGGGCATTTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTCTGGTTCATCTTGG  
TCCATGTGACCGACCGGTGAGATGCCCGGCTCCAGTACGGCCTCCTGATTTTTGGTGCTGCT  
GTCTCTGTCTTCTACAGGAGGTGTTCCGCTTTGCCTACTACAAGCTGCTTAAGAAGGCAGA  
TGAAGGGTTAGCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCCGCCAGATGGCCT  
ATGTTTCTGGTCTCTCCTTCGGTATCATCAGTGGTGTCTTCTCTGTTATCAATATTTTGGCT  
GATGCACTTGGGCCAGGTGTGGTTGGGATCCATGGAGACTCACCTATTACTTCTGACTTC  
AGCCTTTCTGACAGCAGCCATTATCCTGCTCCATACCTTTTGGGGAGTTGTGTTCTTTGATG  
CCTGTGAGAGGAGACGGTACTGGGCTTTGGGCCTGGTGGTTGGGAGTCACCTACTGACATCG  
GGACTGACATTCTGAACCCCTGGTATGAGGCCAGCCTGCTGCCCATCTATGCAGTCACTGT  
TTCCATGGGGCTCTGGGCCTTCATCACAGCTGGAGGGTCCCTCCGAAGTATTCAGCGCAGCC  
TCTTGTGTAAGGACT**TGA**CTACCTGGACTGATCGCCTGACAGATCCCACCTGCCTGTCCACTG  
CCCATGACTGAGCCCAGCCCCAGCCCCGGGTCCATTGCCACATTCTCTGTCTCCTTCTCGTC  
GGTCTACCCCACTACCTCCAGGGTTTTGCTTTGTCTTTTGTGACCGTTAGTCTCTAAGCTT  
TACCAGGAGCAGCCTGGGTTTCCAGCCAGTCACTGAGTGGTGGGTTTGAATCTGCACTTATCCC  
CACCACCTGGGGACCCCTTGTGTTGTGTCAGGACTCCCCCTGTGTGCTGCTCTGCTCTCAC  
CCTGCCCAAGACTCACCTCCCTTCCCCCTCTGCAGGCCGACGGCAGGAGGACAGTCGGGTGAT  
GGTGTATTCTGCCCTGCGCATCCCACCCGAGGACTGAGGGAACCTAGGGGGGACCCCTGGGC  
CTGGGGTGCCCTCCTGATGTCCTCGCCCTGTATTTCTCCATCTCCAGTTCTGGACAGTGCAG  
GTTGCCAAGAAAAGGGACCTAGTTTAGCCATTGCCCTGGAGATGAAATTAATGGAGGCTCAA  
GGATAGATGAGCTCTGAGTTTCTCAGTACTCCCTCAAGACTGGACATCTTGGTCTTTTTCTC  
AGGCCTGAGGGGGAACCATTTTTGGTGTGATAAATAACCTAAACTGCCTTTTTTTCTTTTTT  
GAGGTGGGGGGAGGGAGGAGGTATATTGGAACCTCTTCTAACCTCCTTGGGCTATATTTCTC  
TCCTCGAGTTGCTCCTCATGGCTGGGCTCATTTTCGGTCCCTTTCTCCTTGGTCCCAGACCTT  
GGGGGAAAGGAAGGAAGTGCATGTTTGGGAACTGGCATTACTGGAACATAATGGTTTTAACCT  
CCTTAACCACCAGCATCCCTCCTCTCCCCAAGGTGAAGTGGAGGGTGCTGTGGTGAGCTGGC  
CACTCCAGAGCTGCAGTGCCACTGGAGGAGTCAGACTACCATGACATCGTAGGGAAGGAGGG  
GAGATTTTTTTGTAGTTTTTAATTGGGGTGTGGGAGGGGCGGGGAGGTTTTCTATAAACTGT  
ATCATTTTCTGCTGAGGGTGGAGTGTCCCATCCTTTTAATCAAGGTGATTGTGATTTTGACT  
AATAAAAAAGAATTTGTAAAAA  
AAA  
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA



220/330

**FIGURE 220**

MGA AVFFGCTFVAFGPAFALFLITVAGDPLRVIIILVAGAFFWLVSLLLASVVWFILVHVTDR  
SDARLQYGLLIFGA AVSVLLQEVFRFAYYKLLKKADEGLASLSEDGRSPISIRQMAYVSGLS  
FGIISGVFSVINILADALGPGVVG I HGDS PYYFLTSAFLTAAIILLHTFWGVVFFDACERRR  
YWALGLVVGSHLLTSGLTFLNPWYEASLLPIYAVTVSMGLWAFITAGGSLRSIQRSLLCKD

221/330

**FIGURE 221**

AAGCTGGTTTAAGGAAGCAGAGGAGGGTTAGATTCGTTGAGTGAGGACGGAAGATCAACCCA  
TTTCCATTCCGCCAGATGGCCTATGTTTCTGGTCTCTCCCTTCGGNATCATCAGTGGTGTNT  
TNTCTGTTATCAATATTTTGGCTGATGCANTTGGGCCAGGTGTGGTTGGGATCCATGGAGAC  
TCACCCTATTANTTCCTGANTTCAGCCTTTNTGACAGCAGCCATTATCCTGCTC

222/330

**FIGURE 222**

GACCGACCGTTCAGATGCCCCGGTTCCAGTACGGCTTCCTGATTTTTGGTGCTGCTGTNTCTG  
TCCTTCTACAGGAGGTGTTCCGCTTTGCCTANTACAAGCTGCTTAAGAAGGCAGATGAGGGG  
TTAGCATNGCTGAGTGAGGACGGAAGATCACCCATTTCCATCCGCCAGATGGCCTATGTTTN  
TGGTNTTTCCTTCGGTATCATCAGTGGTGTTTTNTCTGTTATCAATATTTGGNTGATGCAN  
TTGGGCCAGGTGTGGTTGGGATCCATGGAGANTCACCTATTAATTCCTGAATTCAGCCTTT  
NTGACAGCAGCCATTATCCTGNTCCATACCTTTTGGGGAGTTGTGTTTTTTGATGCCTGTGA  
GAGGAG

223/330

**FIGURE 223**

NGTTGGAGAAGTGGCGCGGACNTTCATTTGGGGTTTCGGTTTCCCCCCTTCCCTTTCCCCG  
GGGTCTGGGGTGACATTGCACGGGCCCCCTCGTGGGGTCGCGTTGCCACCCACGCGGACTCC  
CCAGNTGGNGCGCCCTTCCCATTTGCCTGTCCTGGTCAGGCCCCACCCCCCTTCCACNTG  
ACCAGCCATGGGGGCTGCGGTGTTTTTCGGCTGCACTTTCGTCGCGTTCGGCCCGGCCTTCG  
CGCTTTTCTTGATCACTGTGGCTGGGGACCCGCTTCGCGTTATCATCCTGGTCGCAGGGGCA  
TTTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTCTGGTTCATCTTGGTCCATGTGAC  
CGACCGGTCAGATGCCCGGCTCCAGTACGGCCTCCTGATTTTTGGTGCTGCTGTCTCTGTCC  
TTCTACAGGAGGTGTTCCGCTTTGCCTACTACAAGCTGCTTAAGAAGGCAGATGAGGGGTTA  
GCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCCGCCAGATGGCCTATGTTTCTGG  
TCTCTCCTTCGGTATCATCAGTGGTGTCTTCTCTGTTATCAATATTTGGCTGATGCACTTG  
GGCCAGGTGTGGTTGGGATCCATGGAGACTCACCC

224/330

**FIGURE 224**

GTAAAAGAAAGTGGCCGGACCTTCATTGGGGTTTCGGTTCCCCCCTTCCCNTTCCCCGGGG  
TCTGGGGGTGACATTGCACCGCGCCCNCTCGTGGGGTCGCGTTGCCACCCACGCGGACTCCC  
CAGNTGGCGCGCCCCCTCCCATTTGCCTGTCCTGGTCAGGCCCCCACCCTTCCCACCTGA  
CCAGCCATGGGGGCTGCGGTGTTTTTCGGGCTGCACTTTCGTCGCGTTCGGGCCCGGCCTTC  
GCGCTTTTCTTGATCACTGTGGCTGGGGACCCGCTTCGCGTTATCATCCTGGTCGCAGGGGC  
ATTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTCTGGTTCATCTTGGTCCATGTGA  
CCGACCGGTCAGATGCCCCGGCTCCAGTACGGCCTCCTGATTTTGGTGCTGCTGTCTCTGTC  
CTTCTACAGGAGGTGTTCCGCTTTGCCTACTACAAGCTGCTTAAGAAGGCAGATGAGGGGTT  
AGCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCCGCCAGATGGCCTATGTTTCTG  
GTCTCTCCTTCGGTATCATCAGTGGTGTCTTCTCTGTTATCAATATTTTGGCTGATGCACTT  
GGGCCAGGTGTGGTTGGGATCCATGGAGAC

225/330

**FIGURE 225**

GCCCCAGGGAGCAGTGGGTGGTTATAACTCAGGCCCCGGTGCCCAGAGCCCAGGAGGAGGCAG  
TGGCCAGGAAGGCACAGGCCTGAGAAGTCTGCGGCTGAGCTGGGAGCAAATCCCCACCCCC  
TACCTGGGGGACAGGGCAAGTGAGACCTGGTGAGGGTGGCTCAGCAGGCAGGGAAGGAGAGG  
TGTCTGTGCGTCCTGCACCCACATCTTTCTCTGTCCCCTCCTTGCCCTGTCTGGAGGCTGCT  
AGACTCCTATCTTCTGAATTCTATAGTGCCTGGGTCTCAGCGCAGTGCCGATGGTGGCCCCGT  
CCTTGTGGTTCCTCTCTACCTGGGGAAATAAGGTGCAGCGGCC**ATG**GCTACAGCAAGACCCC  
CCTGGATGTGGGTGCTCTGTGCTCTGATCACAGCCTTGCTTCTGGGGGTACAGAGCATGTT  
CTCGCCAACAATGATGTTTCCTGTGACCACCCCTCTAACACCGTGCCCTCTGGGAGCAACCA  
GGACCTGGGAGCTGGGGCCGGGAAGACGCCCGGTCGGATGACAGCAGCAGCCGCATCATCA  
ATGGATCCGACTGCGATATGCACACCCAGCCGTGGCAGGCCGCGCTGTTGCTAAGGCCCAAC  
CAGCTCTACTGCGGGGCGGTGTTGGTGCATCCACAGTGGCTGCTCACGGCCGCCCACTGCAG  
GAAGAAAGTTTTAGAGTCCGTCTCGGCCACTACTCCCTGTCACCAGTTTATGAATCTGGGC  
AGCAGATGTTCCAGGGGGTCAAATCCATCCCCACCCCTGGCTACTCCCACCCTGGCCACTCT  
AACGACCTCATGCTCATCAAACGAACAGAAGAATTCGTCCCACTAAAGATGTCAGACCCAT  
CAACGTCTCCTCTCATTGTCCCTCTGCTGGGACAAAGTGCTTGGTGTCTGGCTGGGGGACAA  
CCAAGAGCCCCCAAGTGCACTTCCCTAAGGTCCTCCAGTGCTTGAATATCAGCGTGCTAAGT  
CAGAAAAGGTGCGAGGATGCTTACCCGAGACAGATAGATGACACCATGTTCTGCGCCGGTGA  
CAAAGCAGGTAGAGACTCCTGCCAGGGTGATTCTGGGGGGCCTGTGGTCTGCAATGGCTCCC  
TGCAGGGACTCGTGTCTTGGGGAGATTACCCCTTGTCGCCGGCCCAACAGACCGGGTGTCTAC  
ACGAACCTCTGCAAGTTCACCAAGTGGATCCAGGAAACCATCCAGGCCAACTCC**TGAG**TCAT  
CCCAGGACTCAGCACACCGGCATCCCCACCTGCTGCAGGGACAGCCCTGACACTCCTTTTCAG  
ACCCTCATTCCCTTCCCAGAGATGTTGAGAATGTTTCATCTCTCCAGCCCCTGACCCCATGTCT  
CCTGGACTCAGGGTCTGCTTCCCCACATTGGGCTGACCGTGTCTCTCTAGTTGAACCCTGG  
GAACAATTTCCAAAACGTGTCAGGGCGGGGGTTGCGTCTCAATCTCCCTGGGGCACTTTTCAT  
CCTCAAGCTCAGGGGCCATCCCTTCTCTGCAGCTCTGACCCAAATTTAGTCCCAGAAATAAA  
CTGAGAAGTGGAATAAAAAA

226/330

**FIGURE 226**

MATARPPWMWVLCALITALLLGVTEHVLANNDVSCDHPSNTVPSGSNQDLGAGAGEDARSDD  
SSSRIINGSDCDMHTQPWQAALLLRPNQLYCGAVLVHPQWLLTAAHCRKKVFRVRLGHYSLS  
PVYESGQQMFQGVKSI PHPGYSHPGHSNDLMLIKLNRRIRPTKDVRPINVSSHCP SAGTKCL  
VSGWGTTKSPQVHF PKVLQCLNISVLSQKRCE DAYPRQIDDTMFCAGDKAGRDSCQGDSGGP  
VVCNGSLQGLVSWGDYPCARPNRPGVYTNLCKFTKWIQETIQANS

227/330

**FIGURE 227**

**ATG**GTCAACGACCGGTGGAAGACCATGGGCGGGCGCTGCCCAACTTGAGGACCGGCCGCGCGA  
CAAGCCCGCAGCGGCCGAGCTGCGGGCTACGTGCTGTGCACCGTGCTGCTGGCCCTGGCTGTGC  
TGCTGGCTGTAGCTGTACCCGGTGCCGTGCTCTTCCTGAACCACGCCCACGCGCCGGGCACG  
GCGCCCCACCTGTCGTACGCACTGGGGCTGCCAGCGCCAACAGCGCCCTGGTCACTGTGGA  
AAGGGCGGACAGCTCGCACCTCAGCATCCTCATTGACCCGCGCTGCCCCGACCTCACCAGACA  
GCTTCGCACGCCTGGAGAGCGCCCAGGCCCTCGGTGCTGCAGGCGCTGACAGAGCACCAGGCC  
CAGCCACGGCTGGTGGGCGACCAGGAGCAGGAGCTGCTGGACACGCTGGCCGACCAGCTGCC  
CCGGCTGCTGGCCCGAGCCTCAGAGCTGCAGACGGAGTGCATGGGGCTGCGGAAGGGGCATG  
GCACGCTGGGCCAGGGCCTCAGCGCCCTGCAGAGTGAGCAGGGCCGCTCATCCAGCTTCTC  
TCTGAGAGCCAGGGCCACATGGCTCACCTGGTGAACCTCCGTACGCGACATCCTGGATGCCCT  
GCAGAGGGACCGGGGGCTGGGCCGGCCCCGCAACAAGGCCGACCTTCAGAGAGCGCCTGCCC  
GGGGAACCCGGCCCCGGGGCTGTGCCACTGGCTCCCGGCCCGAGACTGTCTGGACGTCCTC  
CTAAGCGGACAGCAGGACGATGGCGTCTACTCTGTCTTTCCACCCACTACCCGGCCGGCTT  
CCAGGTGTACTGTGACATGCGCACGACGCGCGCGCTGGACGGTGTTCAGCGCCGGGAGG  
ACGGCTCCGTGAACCTTCTCCGGGGCTGGGACGCGTACCGAGACGGCTTTGGCAGGCTCACC  
GGGGAGCACTGGCTAGGGCTCAAGAGGATCCACGCCCTGACCACACAGGCTGCCTACGAGCT  
GCACGTGGACCTGGAGGACTTTGAGAATGGCACGGCCTATGCCCGCTACGGGAGCTTCGGCG  
TGGGCTTGTCTCCGTGGACCCTGAGGAAGACGGGTACCCGCTCACCCTGGCTGACTATTCC  
GGCACTGCAGGCGACTCCCTCCTGAAGCACAGCGGCATGAGGTTACCAACCAAGGACCCGTGA  
CAGCGACCATTCAGAGAACAACCTGTGCCGCCCTTCTACCGCGGTGCCTGGTGGTACCGCAACT  
GCCACACGTCCAACCTCAATGGGCAGTACCTGCGCGGTGCGCACGCCTCCTATGCCGACGGC  
GTGGAGTGGTCCTCCTGGACCGGCTGGCAGTACTCACTCAAGTTCTCTGAGATGAAGATCCG  
GCCGGTCCGGGAGGACCGCT**TAG**ACTGGTGCACCTTGTCTTGGCCCTGCTGGTCCCTGTGCG  
CCCATCCCCGACCCACCTCACTCTTTCGTGAATGTTCTCCACCCACCTGTGCCCTGGCGGAC  
CCACTCTCCAGTAGGGAGGGGCCGGCCATCCCTGACACGAAGCTCCCTGGGCCGGTGAAGT  
CACACATCGCCTTCTCGCCGTCCCCACCCCTCCATTTGGCAGCTCACTGATCTCTTGCCTC  
TGCTGATGGGGGCTGGCAAACCTTGACGACCCCAACTCCTGCCTGCCCCACTGTGACTCCGG  
TGCTGTTTGGCGTCCCCCTGGCCAGGATGGTGGAGTCTGCCCCAGGCACCCCTCTGCCCTGCCC  
GGCCAAATACCCGGCATTATGGGGACAGAGACAGGGGGCAGACAGACCCCTGGAGTCTCTC  
CTAGCAGATCGTGGGAATGTCAAGGTCTCTCTGAGGTCAGGTCTGAGGCCAGTATCCTCCAG  
CCCTCCCAATGCCAACCCCCACCCGTTTCCCTGGTGCCAGAGAACCCACCTCTCCCCCAA  
GGGCCTCAGCCTGGCTGTGGGCTGGGTGGCCCCATCCTACCAGGCCCTGAGGTCAGGATGGG  
GAGCTGCTGCCTTTGGGGACCCACGCTCCAAGGCTGAGACCAGTTCCTTGGAGGCCACCCAC  
CCTGTGCCCCGGCAGGCCTGGGGTCTGCAGTCTCTTACCTGCTGTGCCCACCTGCTCTCTG  
TCTCAAATGAGGCCCAACCCATCCCCACCCAGCTCCCGGCCGTCTCCTACCTGGGGCAGC  
CGGGGCTGCCATCCCATTTCTCCTGCCTCTGGAAGGTGGGTGGGGCCCTGCACCGTGGGGCT  
GGACTGCGCTAATGGGAAGCTCTTGGTTTTCTGGGCTGGGGCCTAGGCAGGGCTGGGATGAG  
GCTTGTACAACCCCCACCACCAATTTCCCAGGGACTCCAGGGTCTGAGGCCTCCCAGGAGG  
GCCTTGGGGGTGATGACCCCTTCCCTGAGGTGGCTGCTCTCATGAGGAGGCCAACCCTTGCC  
ATTGACCGTGGCCACCTGGACCCAGGCCAGGCCCGGCCGCGAGTGGTCAAGGGACAGGGA  
CCACCTCACCGGGCAAATGGGGTGGGGGGGACTGGGGCACCAGACCAGGCACCACTGGACA  
CTTTCTTGTGAATCCTCCCAACACCCAGCACGCTGTCATCCCCACTCCTTGTGTGCACACA  
TGCAGAGGTGAGACCCGCGAGGCTCCCAGGACCAGCACCAAGGGCAGGGCTGGAGCCGGG  
TCCTCAGCTGTCTGCTCAGCAGCCCTGGACCCCGCTGCGTTACGTACGGCCAGATGCAGGG  
CGGCTTTTCCAAGGCCTCCTGATGGGGGGCTCCGAAAGGGCTGGAGTCAGCCTTGGGGAGCT  
GCCTAGCAGCCTCTCCTCGGGCAGGAGGGGAGGTGGCTTCTCCTCAAAGGACACCCGATGGCA  
GGTGCCTAGGGGGTGTGGGGTTCCGTTCTCCCTTCCCTCCCACTGAAGTTTGTGCTTAAAA  
AACAAATAAATTTGACTTGGCACCACTGGGGGTTGGTGGGAGAGGCCGTGTGACCTGGCTCTC  
TGTCCAGTGCCACCAGGTCATCCACATGCGCAG



228/330

**FIGURE 228**

MVNDRWKTMGGAAQLEDPRDPKQRPSCGYVLCTVLLALAVLLAVAVTGAVLFLNHAHAPGT  
APPPVVSTGAASANSALVTVERADSSHLSILIDPRCPDLTDSFARLESAQASVLQALTEHQA  
QPRLVGDQEQELDLADQLPRLLARASELQTECMGLRKHGHTLGQGLSALQSEQGRLLIQLL  
SESQGHMAHLVNSVSDILDALQDRGLGRPRNKADLQRAPARGTRPRGCATGSRPRDCLDVL  
LSGQQDDGVYSVFPTHYPAGFQVYCDMRTDGGGWTVFQRREDGSVNFFRGWDAYRDGFGRLT  
GEHWLGLKRIHALTTQAAYELHVDLED FENG TAYARYGSFGVGLFSVDPEEDGYPLTVADYS  
GTAGDSLLKHSGMRFTTKDRSDHSENNCAAFYRGAWWYRNCHTSNLNGQYLRGAHASADG  
VEWSSWTGWQYSLKFSEM KIRPVREDR

229/330

**FIGURE 229**

GCAGTCAGAGACTTCCCCTGCCCCTCGCTGGGAAAGAACATTAGGAATGCCTTTTAGTGCCCT  
TGCTTCCTGAACTAGCTCACAGTAGCCCGGCGGCCAGGGCAATCCGACCACATTTCACTCT  
CACCGCTGTAGGAATCCAG**ATG**CAGGCCAAGTACAGCAGCACGAGGGACATGCTGGATGATG  
ATGGGGACACCACCATGAGCCTGCATTCTCAAGCCTCTGCCACAACCTCGGCATCCAGAGCCC  
CGGCGCACAGAGCACAGGGCTCCCTCTTCAACGTGGCGACCAGTGGCCCTGACCCTGCTGAC  
TTTGTGCTTGGTGCTGCTGATAGGGCTGGCAGCCCTGGGGCTTTTGTTTTTTTCAGTACTACC  
AGCTCTCCAATACTGGTCAAGACACCATTTCTCAAATGGAAGAAAGATTAGGAAATACGTCC  
CAAGAGTTGCAATCTCTTCAAGTCCAGAATATAAAGCTTGCAGGAAGTCTGCAGCATGTGGC  
TGAAAAACTCTGTCTGTAGCTGTATAACAAAGCTGGAGCACACAGGTGCAGCCCTTGTACAG  
AACAAATGGAAATGGCATGGAGACAATTGCTACCAGTTCTATAAAGACAGCAAAAGTTGGGAG  
GACTGTAAATATTTCTGCCTTAGTGAAAACCTCTACCATGCTGAAGATAAACAAACAAGAAGA  
CCTGGAATTTGCCGCGTCTCAGAGCTACTCTGAGTTTTTCTACTCTTATTGGACAGGGCTTT  
TGCGCCCTGACAGTGGCAAGGCCTGGCTGTGGATGGATGGAACCCCTTTCACCTCTGAACTG  
TTCCATATTATAATAGATGTCACCAGCCCAAGAAGCAGAGACTGTGTGGCCATCCTCAATGG  
GATGATCTTCTCAAAGGACTGCAAAGAATTGAAGCGTTGTGTCTGTGAGAGAAGGGCAGGAA  
TGGTGAAGCCAGAGAGCCTCCATGTCCCCCTGAAACATTAGGCGAAGGTGACT**TGA**ATTCGCC  
CTCTGCAACTACAAATAGCAGAGTGAGCCAGGCGGTGCCAAAGCAAGGGCTAGTTGAGACAT  
TGGGAAATGGAACATAATCAGGAAAGACTATCTCTCTGACTAGTACAAAATGGGTTCTCGTG  
TTTCCTGTTTCAGGATCACCAGCATTTCTGAGCTTGGGTTTATGCACGTATTTAACAGTCACA  
AGAAGTCTTATTTACATGCCACCAACCAACCTCAGAAACCCATAATGTCATCTGCCTTCTTG  
GCTTAGAGATAACTTTTAGCTCTCTTTCTTCTCAATGTCTAATATCACCTCCCTGTTTTTCAT  
GTCTTCCTTACACTTGGTGGAAATAAGAACTTTTTGAAGTAGAGGAAATACATTGAGGTAAC  
ATCCTTTTCTCTGACAGTCAAGTAGTCCATCAGAAATTGGCAGTCACTTCCCAGATTGTACC  
AGCAAATACACAAGGAATTCTTTTTGTTTGTTTCAGTTCATACTAGTCCCTTCCCAATCCAT  
CAGTAAAGACCCCATCTGCCTTGTCATGCCGTTTCCCAACAGGGATGTCACTTGATATGAG  
AATCTCAAATCTCAATGCCTTATAAGCATTCCTTCCTGTGTCCATTAAGACTCTGATAATTG  
TCTCCCCTCCATAGGAATTTCTCCCAGGAAAGAAATATATCCCCATCTCCGTTTCATATCAG  
AACTACCGTCCCCGATATTCCCTTCAGAGAGATTAAAGACCAGAAAAAAGTGAGCCTCTTCA  
TCTGCACCTGTAATAGTTTCAGTTCCTATTTTCTTCCATTGACCCATATTTATACCTTTCAG  
GTACTGAAGATTTAATAATAATAAATGTAAATACTGTGAAAAA

230/330

**FIGURE 230**

MQAKYSSTRDMLDDDGDTTMSLHSQASATTRHPEPRRTEHRAPSSSTWRPVALTLLTLCVL  
LLIGLAALGLLFFQYYQLSNTGQDTISQMEERLGNTSQELQSLQVQNIKLAGSLQHVAEKLCRE  
LYNKAGAHRCSPCTEQWKWHGDNCYQFYKDSKSWEDCKYFCLSENSTMLKINKQEDLEFAAS  
QSYSEFFYSYWTGLLRPDSGKAWLWMDGTPFTSELFHIIIDVTSPRSRDCVAILNGMIFSKD  
CKELKRCVCERRAGMVKPESLHVPPETLGEGD

231/330

**FIGURE 231**

AATTTTCACCGCTGTAGGAATCCAGATGCAGGCCAAGTACAGCAGCACGAGGGACATGNTGG  
ATGATGATGGGACACCACCATGAGCCTGCATTNTCAAGCTTTTGCCACAATTCGGCATCCAG  
AGCCCCGGCGCACAGAGCACAGGGNTCCTTTTTCAACGTGGCGACCAGTGGCCCTGACCCTG  
CTGACTTTGTGCTTGGTGCTGCTGATAGGGCTGGCAGCCCTGGGGCTTTTGTTTTTTCAGTA  
CTACCAGCTCTCCAATACTGGTCAAGACACCATTTCTCAAATGGAAGAAAGATTAGGAAATA  
CGTCCCAAGAGTTGCAATTTNTTCAAGTCCAGAATATAAAGCTTGCAGGAAGTNTGCAGCAT  
GTGGCTGAAAAACTCTGTCGTGAGCTGTATAACAAAGCTGGAGGAACTTTGAAGGAGGGCAA  
AGTNTCCTCATNTACTATACACACACCACTTCCC

232/330

**FIGURE 232**

GCCGAGCGCAAGAACCCTGCGCAGCCCAGAGCAGCTGCTGGAGGGGAATCGAGGCGCGGCTC  
CGGGGATTCGGCTCGGGCCGCTGGCTCTGCTCTGCGGGGAGGGAGCGGGCCCGCGCGGG  
CCCGAGCCCTCCGGATCCGCCCCCTCCCGGTCCCGCCCCCTCGGAGACTCCTCTGGCTGCT  
CTGGGGGTTCGCCGGGGCCGGGGACCCGCGGTCCGGGCGCC**ATG**CGGGCATCGCTGCTGCTG  
TCGGTGCTGCGGCCCCGAGGGCCCGTGGCCGTGGGCATCTCCCTGGGCTTCACCCTGAGCCT  
GCTCAGCGTCACCTGGGTGGAGGAGCCGTGCGGCCCAGGCCCGCCCCAACCTGGAGACTCTG  
AGCTGCCGCCGCGCGGCAACACCAACGCGCGCGCCGCCAACCTCGGTGCAGCCCCGAGCG  
GAGCGCGAGAAGCCCCGGGGCCGGCGAAGGCGCCGGGGAGAATTGGGAGCCGCGCGTCTTGCC  
CTACCACCCTGCACAGCCCCGGCCAGGCCGCCAAAAAGGCCGTAGGACCCGCTACATCAGCA  
CGGAGCTGGGCATCAGGCAGAGGCTGCTGGTGGCGGTGCTGACCTCTCAGACCACGCTGCCC  
ACGCTGGGCGTGGCCGTGAACCGCACGCTGGGGCACCGGCTGGAGCGTGTGGTGTTCCTGAC  
GGGCGCACGGGGCCGCCGGGCCCCACCTGGCATGGCAGTGGTGACGCTGGGCGAGGAGCGAC  
CCATTGGACACCTGCACCTGGCGCTGCGCCACCTGCTGGAGCAGCACGGCGACGACTTTGAC  
TGGTTCTTCTGGTGCCCTGACACCACCTACACCGAGGCGCACGGCCTGGCACGCCTAACTGG  
CCACCTCAGCCTGGCCTCCGCCGCCACCTGTACCTGGGCCGGCCCCAGGACTTCATCGGCG  
GAGAGCCACCCCCGGCCGCTACTGCCACGGAGGCTTTGGGTGCTGCTGTGCGCATGCTG  
CTGCAACAACCTGCGCCCCACCTGGAAGGTGCCGCAACGACATCGTCAGTGCAGCGCCCTGA  
CGAGTGGCTGGGTGCTGCTGCTGATGCCACCGGGGTGGGCTGCACTGGTGACCACGAGG  
GGGTGCACTATAGCCATCTGGAGCTGAGCCCTGGGGAGCCAGTGCAGGAGGGGGACCCTCAT  
TTCCGAAGTGCCCTGACAGCCCACCCTGTGCGTGACCCTGTGCACATGTACCAGCTGCACAA  
AGCTTTCGCCCGAGCTGAACTGGAACGCACGTACCAGGAGATCCAGGAGTTACAGTGGGAGA  
TCCAGAATACCAGCCATCTGGCCGTTGATGGGGACCGGGCAGCTGCTTGGCCCGTGGGTATT  
CCAGCACCATCCCGCCCGCCTCCCGCTTTGAGGTGCTGCGCTGGGACTACTTCACGGAGCA  
GCACGCTTTCTCTGCGCCGATGGCTCACCCCGCTGCCCACTGCGTGGGGCTGACCGGGCTG  
ATGTGGCCGATGTTCTGGGGACAGCTCTAGAGGAGCTGAACCGCCGCTACCACCCGGCCTTG  
CGGCTCCAGAAGCAGCAGCTGGTGAATGGCTACCGACGCTTTGATCCGGCCCCGGGGTATGGA  
ATACACGCTGGACTTGACAGCTGGAGGCACTGACCCCCAGGGAGGCCCGCCGCCCTCACTC  
GCCGAGTGACAGCTGCTCCGGCCGCTGAGCCGCGTGAGAGATCTTGCCTGTGCCCTATGTCACT  
GAGGCCTCACGTCTCACTGTGCTGCTGCCTCTAGCTGCGGCTGAGCGTGACCTGGCCCCCTGG  
CTTCTTGGAGGCCTTTGCCACTGCAGCACTGGAGCCTGGTGATGCTGCGGCAGCCCTGACCC  
TGCTGCTACTGTATGAGCCGCGCCAGGCCCAGCGCTGGCCCATGCAGATGTCTTCGCACCT  
GTCAAGGCCACGTGGCAGAGCTGGAGCGGCGTTTCCCGGTGCCCGGGTGCCATGGCTCAG  
TGTGCAGACAGCCGCACCCCTCACCACTGCGCCTCATGGATCTACTCTCCAAGAAGCACCCGC  
TGGACACACTGTTCTGTGGCCGGGCCAGACACGGTGCTCACGCCTGACTTCCTGAACCGC  
TGCCGCATGCATGCCATCTCCGGCTGGCAGGCCTTCTTTCCCATGCATTTCCAAGCCTTCCA  
CCCAGGTGTGGCCCCACCACAAGGGCCTGGGCCCCAGAGCTGGGCCGTGACACTGGCCGCT  
TTGATCGCCAGGCAGCCAGCGAGGCCTGCTTCTACAACCTCCGACTACGTGGCAGCCCGTG  
CGCCTGGCGGCAGCCTCAGAACAAGAAGAGGAGCTGCTGGAGAGCCTGGATGTGTACGAGCT  
GTTCTCTCACTTCTCCAGTCTGCATGTGCTGCGGGCGGTGGAGCCGGCGCTGCTGCAGCGCT  
ACCGGGCCCAGACGTGCAGCGCGAGGCTCAGTGAGGACCTGTACCACCGCTGCCTCCAGAGC  
GTGCTTGAGGGCCTCGGCTCCCGAACCCAGCTGGCCATGCTACTCTTTGAACAGGAGCAGGG  
CAACAGCACCT**TGA**CCCCACCCTGTCCCGTGGGCCGTGGCATGGCCACACCCCACTT  
CTCCCCAAAACCAGAGCCACCTGCCAGCCTCGCTGGGCAGGGCTGGCCGTAGCCAGACCCC  
AAGCTGGCCCCACTGGTCCCCCTCTCTGGCTCTGTGGGTCCCTGGGCTCTGGACAAGCACTGGG  
GGACGTGCCCCCAGAGCCACCCACTTCTCATCCCAAACCCAGTTTCCCTGCCCCCTGACGCT  
GCTGATTGCGGCTGTGGCCTCCACGTATTTATGCAGTACAGTCTGCCTGACGCCAGCCCTGC  
CTCTGGGCCCTGGGGCTGGGCTGTAGAAGAGTTGTTGGGAAGGAGGAGCTGAGGAGGG  
GCATCTCCCAACTTCTCCCTTTTGGACCCTGCCGAAGCTCCCTGCCTTTAATAAACTGGCCA  
AGTGTGGAAAAA

233/330

**FIGURE 233**

MRASLLLSVLRPAGPVAVGISLGFTLSLLSVTWVEEPCGPGPPQPGDSELPPRGNTNAARRP  
NSVQPGAEREKPGAGEGAGENWEPRVLPYHPAQPGQAAKKAVRTRYISTELGIRQRLLVAVL  
TSQTTLPTLGVAVNRTLGHRLERVVFLTGARGRRAPPGMAVVTLGEERPIGHLHLALRHLL  
QHGDDEFDWFFLVDPDTTYTEAHGLARLTGHLSLASAAHLYLGRPQDFIGGEPTPGRYCHGGFG  
VLLSRMLLQQLRPHLEGCRNDIVSARPDEWLGRCIL DATGVGCTGDHEGVHYSHLELSPGEP  
VQEGDPHFERSALTAHPVRDPVHMYQLHKAFARAELETTYQEIQELQWEIQNTSHLAVDGDRA  
AAWPVGIPAPSRPASRFVLRWDYFTEQHAFSCADGSPRCPLRGADRADVADVLGTALEELN  
RRYHPALRLQKQQLVNGYRRFDPARGMEYTLDLQLEALTPQGGRRPLTRRVQLLRPLSRVEI  
LPVPYVTEASRLTVLLPLAAAERDLAPGFLEAFATAALEPGDAAAALTLLLLYEPRQAQRVA  
HADVFAPVKAHVAELERRFPGARVPWLSVQTAAPSPLRLMDLLSKKHPLDTLFLLAGPDTVL  
TPDFLNRCRMHAISGWQAFFPMHFQAFHPGVAPPQGPPELGRDTGRFDRQAASEACFYNS  
DYVAARGRLAAASEQEEELLES LDVYELFLHFSSLHVLRAVEPALLQRYRAQTCSARLSEDL  
YHRCLQSVLEGLGSRTQLAMLLFEQE QGNST

234/330

**FIGURE 234**

GCTCTGGCCGGCCCCGGCGATTGGTCACCGCCCGCTAGGGGACAGCCCTGGCCTCCTCTGAT  
TGGCAAGCGCTGGCCACCTCCCCACACCCCTTGCGAACGCTCCCCTAGTGGAGAAAAGGAGT  
AGCTATTAGCCAATTTCGGCAGGGCCCGCTTTTTAGAAAGCTTGATTTCCCTTTGAAGATGAAAG  
ACTAGCGGAAGCTCTGCCTCTTTCCCCAGTGGGCGAGGGAACTCGGGGCGATTGGCTGGGAA  
CTGTATCCACCCAAATGTCACCGATTTCCTTCCTATGCAGGAAATGAGCAGACCCATCAATAA  
GAAATTTCTCAGCCTGGCCGAAAATGGTTGGCCCCACGAAGCCACGACAACCTGGAGGCCAAAG  
AGGGTTGCTCAACGCCCCGCCTCATTGGAAAACCAAATCAGATCTGGGACCTATATAGCGTG  
GCGGAGGCGGGGCGATGATTGTCGCGCTCGCACCCACTGCAGCTGCGCACAGTCGCATTTCT  
TTCCCCGCCCCCTGAGACCCTGCAGCACCATCTGT**CATG**GCGGCTGGGCTGTTTGGTTTGAGC  
GCTCGCCGTCTTTTGGCGGCAGCGGCGACGCGAGGGCTCCCGGCCGCCCGCGTCCGCTGGGA  
ATCTAGCTTCTCCAGGACTGTGGTCGCCCCGTCCGCTGTGGCGGGAAAGCGGCCCCCAGAAC  
CGACCACACCGTGGCAAGAGGACCCAGAACCCGAGGACGAAAACCTTGTATGAGAAGAACCCA  
GACTCCCATGGTTATGACAAGGACCCCGTTTTGGACGTCTGGAACATGCGACTTGTCTTCTT  
CTTTGGCGTCTCCATCATCCTGGTCCTTGGCAGCACCTTTGTGGCCTATCTGCCTGACTACA  
GGATGAAAGAGTGGTCCCGCCGCGAAGCTGAGAGGCTTGTGAAATACCGAGAGGCCAATGGC  
CTTCCCATCATGGAATCCAACCTGCTTCGACCCCAGCAAGATCCAGCTGCCAGAGGATGAG**TG**  
**A**CCAGTTGCTAAGTGGGGCTCAAGAAGCACCGCCTTCCCCACCCCCTGCCTGCCATTCTGAC  
CTCTTCTCAGAGCACCTAATTAAAGGGGCTGAAAGTCTGAA

235/330

**FIGURE 235**

MAAGLFGLSARRLLAAAATRGLPAARVRWESSFSRTVVAPSAVAGKRPPEPTTPWQEDPEPE  
DENLYEKNPDSHGYDKDPVLDVWNMRLVFFFGVSIILVLGSTFVAYLPDYRMKEWSRREAER  
LVKYREANGLPIMESNCFDPSKIQLPEDE



236/330

**FIGURE 236**

GGCGGCTGGGCTGTTTGGTTTGAGCGCTCGCCGTCTTTTGGCGGCAGCGGCGACGCGAGGGC  
TCCCGGCCGCCCCGCGTCCGCTGGGAATCTAGCTTCTCCAGGACTGTGGTCGCCCCGTCCGCT  
GTGGCGGGAAAGCGGCCCCCAGAACCGACCACACCGTGGCAAGAGGACCCAGAACCCGAGGA  
CGAAAACCTTGTATGAGAAGAACCCAGACTCCCATGGTTATGACAAGGACCCCGTTTTGGACG  
TCTGGAACATGCGACTTGTCTTCTTCTTTGGCGTCTCCATCATCCTGGTCCTTGGCAGCACC  
TTTGTGGCCTATCTGCCTGACTACAGGATGAAAGAGTGGTCCCGCCGCGAAGCTGAGAGGCT  
TGTGAAATACCGAGAGGCCAATGGCCTTCCCATCATGGAATCCAACCTGCTTCGACCCCAGCA  
AGATCCAG

237/330

**FIGURE 237**

GCGGCGGCT**ATG**CCGCTTGCTCTGCTCGTCCTGTTGCTCCTGGGGCCCGGCGGCTGGTGCCT  
TGCAGAACCCCCACGCGACAGCCTGCGGGAGGAACTTGTCATCACCCCGCTGCCTTCCGGGG  
ACGTAGCCGCCACATTCCAGTTCCGCACGCGCTGGGATTTCGGAGCTTCAGCGGGAAGGAGTG  
TCCCATTACAGGCTCTTTCCCAAAGCCCTGGGGCAGCTGATCTCCAAGTATTCTCTACGGGA  
GCTGCACCTGTCATTACACAAAGGCTTTTGGAGGACCCGATACTGGGGGCCACCCCTTCCTGC  
AGGCCCCATCAGGTGCAGAGCTGTGGGTCTGGTTCCAAGACACTGTCAGTGTGGATAAA  
TCTTGGAAGGAGCTCAGTAATGTCCTCTCAGGGATCTTCTGCGCCTCTCTCAACTTCATCGA  
CTCCACCAACACAGTCACTCCCACTGCCTCCTTCAAACCCCTGGGTCTGGCCAATGACACTG  
ACCACTACTTTCTGCGCTATGCTGTGCTGCCGCGGGAGGTGGTCTGCACCGAAAACCTCACC  
CCCTGGAAGAAGCTCTTGCCCTGTAGTTCCAAGGCAGGCCTCTCTGTGCTGCTGAAGGCAGA  
TCGCTTGTTCCACACCAGCTACCACTCCCAGGCAGTGCATATCCGCCCTGTTTGCAGAAATG  
CACGCTGTACTAGCATCTCCTGGGAGCTGAGGCAGACCCTGTCAGTTGTATTTGATGCCTTC  
ATCACGGGGCAGGGAAAGAAAGACTGGTCCCTCTTCCGGATGTTCTCCCGAACCCCTCACGGA  
GCCCTGCCCCCTGGCTTCAGAGAGCCGAGTCTATGTGGACATCACCACTACAACCAGGACA  
ACGAGACATTAGAGGTGCACCCACCCCGACCACTACATATCAGGACGTCATCCTAGGCACT  
CGGAAGACCTATGCCATCTATGACTTGCTTGACACCGCCATGATCAACAACTCTCGAAACCT  
CAACATCCAGCTCAAGTGGAAGAGACCCCCAGAGAATGAGGCCCCCCCAGTGCCCTTCCTGC  
ATGCCCAGCGGTACGTGAGTGGCTATGGGCTGCAGAAGGGGGAGCTGAGCACACTGCTGTAC  
AACACCCACCCATACCGGGCCTTCCCGGTGCTGCTGCTGGACACCGTACCCTGGTATCTGCG  
GCTGTATGTGCACACCCTCACCATCACCTCCAAGGGCAAGGAGAACAAACCAAGTTACATCC  
ACTACCAGCCTGCCCAGGACCGGCTGCAACCCACCTCCTGGAGATGCTGATTCAGCTGCCG  
GCCAACTCAGTCACCAAGGTTTCCATCCAGTTTGAGCGGGCGCTGCTGAAGTGGACCGAGTA  
CACGCCAGATCCTAACCATGGCTTCTATGTCAGCCCATCTGTCCTCAGCGCCCTTGTGCCCA  
GCATGGTAGCAGCCAAGCCAGTGGACTGGGAAGAGAGTCCCCTCTTCAACAGCCTGTTCCCA  
GTCTCTGATGGCTCTAACTACTTTGTGCGGCTCTACACGGAGCCGCTGCTGGTGAACCTGCC  
GACACCGGACTTCAGCATGCCCTACAACGTGATCTGCCTCACGTGCACTGTGGTGGCCGTGT  
GCTACGGCTCCTTCTACAATCTCCTCACCCGAACCTTCCACATCGAGGAGCCCCGCACAGGT  
GGCCTGGCCAAGCGGCTGGCCAACCTTATCCGGCGCGCCCGAGGTGTCCCCCACTCT**TGAT**T  
CTTGCCCTTTCCAGCAGCTGCAGCTGCCGTTTCTCTCTGGGGAGGGGAGCCCAAGGGCTGTT  
TCTGCCACTTGCTCTCCTCAGAGTTGGCTTTTGAACCAAAGTGCCCTGGACCAGGTCAGGGC  
CTACAGCTGTGTTGTCCAGTACAGGAGCCACGAGCCAAATGTGGCATTTGAATTTGAATTAA  
CTTAGAAATTCATTTCTCACCTGTAGTGGCCACCTCTATATTGAGGTGCTCAATAAGCAAA  
AGTGGTCGGTGGCTGCTGTATTGGACAGCACAGAAAAAGATTTCCATCACACAGAAAGGTC  
GGCTGGCAGCACTGGCCAAGGTGATGGGGTGTGCTACACAGTGTATGTCAGTGTGTAGTGA  
TGGAGTTTACTGTTTGTGGAATAAAAACGGCTGTTTCCGTGGAAAAA

238/330

**FIGURE 238**

MPLALLVLLLLGPGGWCLAEP PRDSLREELVITPLPSGDVAATFQFRTRWDSELQREGVSHY  
RLF PKALGQLISKYSLRELHLSFTQGFWRTRYWGPPFLQAPSGAELWVWFQDTVTDV D KSWK  
ELSNVLSGIFCASLNFIDSTNTVTPTASF KPLGLANDTDHYFLRYAVLPREVVCTENLTPWK  
KLLPCSSKAGLSVLLKADRLFHTSYHSQAVHIRPVCRNARCTSI SWELRQTL SVVFDAFITG  
QGKKDWSLFRMF SRTLTEPCPLASESRVYVDITTYNQDNETLEVHPPPTTTYQDVILGTRKT  
YAIYDLLDTAMINNSRNLNIQLKWKRP PENEAPPVPFLHAQRYVSGYGLQKGELSTLLYNTH  
PYRAFPVLLLDTPWYLRLYVHTLTITSKGKENKPSYIHYQPAQDRLQPHLLEMLIQLPANS  
VTKVSIQFERALLKWTEYTPDPNHGFYVSPSVLSALVPSMVAAPVDWEESPLFNSLFPVSD  
GSNYFVRLYTEPLL VNLPTPDFSMPYNVICLTCTVAVCYGSFYNLLTRTFHIEEPRTGGLA  
KRLANLIRRARGVPPL

239/330

**FIGURE 239**

CAAC**ATG**GGGTCCAGCAGCTTCTTGGTCCTCATGGTGTCTCTCGTTCTTGTGACCCTGGTGG  
CTGTGGAAGGAGTTAAAGA<sup>5</sup>GGTATAGAGAAAGCAGGGGTTTGCCCAGCTGACAACGTACGC  
TGCTTCAAGTCCGATCCTCCCCAGTGTCACACAGACCAGGACTGTCTGGGGGAAAGGAAGTG  
TTGTTACCTGCACTGTGGCTTCAAGTGTGTGATTCTGTGAAGGAACTGGAAGAAGGAGGAA  
ACAAGGATGAAGATGTGTCAAGGCCATACCCTGAGCCAGGATGGGAGGCCAAGTGTCCAGGC  
TCCTCCTCTACCAGGTGTCCTCAGAAAT**TGA**TGCTGGGTCTTTCTACCTCTGGGGGTCACTC  
TCACTTGGCACCTGCCCCTGAGGGTCCTGAGACTTGGAATATGGAAGAAGCAATACCCAACC  
CCACCAAAGAAAACCTGAGCTTGAAGTCCTTTTCCCCAAAAGAGGGAAGAGTCACAAAAG  
TCCAGACCCCAGGGACGGTACTTTCCCTCTCTACCTGGTGCTCCTCCCTAATGCTCATGAAT  
GGACCCCTCATGAATGAAACCAGTGCCCTTATAAGAGACCCCAAAGAGCTGCCTTGCCCTTC  
TGCAATGTGTGATCACAGCTAGAAGGCACTGTCAGAGAAGAGAACTGGTCCTCACCAGATG  
CTGAATCTGCTGGTGCCTTGATCTTGGACTTCCCAGCCTCTAGAACTGTAAGAAATAAATAT  
TTGCTGTTTATAATCCAA

240/330

**FIGURE 240**

MGSSSFVLVLMVSLVLVTLVAVEGVKEGIEKAGVCPADNVRCFKSDPPQCHTDQDCLGERKCC  
YLHCGFKCVIPVKELEEGGNKDEDVSRPYPEPGWEAKCPGSSSTRCPQK

**Signal sequence:**

amino acids 1-19

**N-myristoylation sites:**

amino acids 23-29, 27-33, 32-38, 102-108

**WAP-type 'four-disulfide core' domain signature:**

amino acids 49-63

241/330

**FIGURE 241**

AAACTCAGCACTTGCCGGAGTGGCTCATTGTTAAGACAAAGGGTGTGCACTTCCTGGCCAGG  
AAACCTGAGCGGTGAGACTCCCAGCTGCCTACATCAAGGCCCCAGGACATGCAGAACCTTCC  
TCTAGAACCCGACCCACCACC**ATG**AGGTCTGCTGTGGAGATGCAGGCACCTGAGCCAAGG  
CGTCCAGTGGTCCTTGCTTCTGGCTGTCCTGGTCTTCTTTCTCTTCGCCTTGCCCTCTTTTA  
TTAAGGAGCCTCAAACAAAGCCTTCCAGGCATCAACGCACAGAGAACATTAAAGAAAGGTCT  
CTACAGTCCCTGGCAAAGCCTAAGTCCCAGGCACCCACAAGGGCGAGGAGGACAACCATCTA  
TGCAGAGCCAGCGCCAGAGAACAAATGCCCTCAACACACAAACCCAGCCCAAGGCCACACCA  
CCGGAGACAGAGGAAAGGAGGCCAACCAGGCACCGCCGGAGGAGCAGGACAAGGTGCCCCAC  
ACAGCACAGAGGGCAGCATGGAAGAGCCCAGAAAAAGAGAAAACCATGGTGAACACACTGTC  
ACCCAGAGGGCAAGATGCAGGGATGGCCTCTGGCAGGACAGAGGCACAATCATGGAAGAGCC  
AGGACACAAAGACGACCCAAGGAAATGGGGGCCAGACCAGGAAGCTGACGGCCTCCAGGACG  
GTGTGAGAGAAGCACCAGGGCAAAGCGGCAACCACAGCCAAGACGCTCATTCCCAAAGTCA  
GCACAGAATGCTGGCTCCACAGGAGCAGTGTCAACAAGGACGAGACAGAAAGGAGTGACCA  
CAGCAGTCATCCCACCTAAGGAGAAGAAACCTCAGGCCACCCACCCCTGCCCTTTCCAG  
AGCCCCACGACGCAGAGAAACCAAGACTGAAGGCCGCCAACTTCAAATCTGAGCCTCGGTG  
GGATTTTGGAGAAAAATACAGCTTCGAAATAGGAGGCCTTCAGACGACTTGCCCTGACTCTG  
TGAAGATCAAAGCCTCCAAGTCGCTGTGGCTCCAGAAACTCTTTCTGCCCAACCTCACTCTC  
TTCCTGGACTCCAGACACTTCAACCAGAGTGAGTGGGACCGCCTGGAACACTTTGCACCACC  
CTTTGGCTTCATGGAGCTCAACTACTCCTTGGTGCAGAAGGTCGTGACACGCTTCCCTCCAG  
TGCCCCAGCAGCAGCTGCTCCTGGCCAGCCTCCCCGCTGGGAGCCTCCGGTGCATCACCTGT  
GCCGTGGTGGGCAACGGGGGCATCCTGAACAACCTCCACATGGGCCAGGAGATAGACAGTCA  
CGACTACGTGTTCCGATTGAGCGGAGCTCTCATTAAAGGCTACGAACAGGATGTGGGGACTC  
GGACATCCTTCTACGGCTTTACCGCCTTCTCCCTGACCCAGTCACTCCTTATATTGGGCAAT  
CGGGGTTTCAAGAACGTGCCTCTTGGGAAGGACGTCCGCTACTTGCACTTCCTGGAAGGCAC  
CCGGGACTATGAGTGGCTGGAAGCACTGCTTATGAATCAGACGGTGATGTCAAAAAACCTTT  
TCTGGTTCAGGCACAGACCCAGGAAGCTTTTCGGGAAGCCCTGCACATGGACAGGTACCTG  
TTGCTGCACCCAGACTTTCTCCGATACATGAAGAACAGGTTTCTGAGGTCTAAGACCCTGGA  
TGGTGCCCACTGGAGGATATACCGCCCCACCACTGGGGCCCTCCTGCTGCTCACTGCCCTTC  
AGCTCTGTGACCAGGTGAGTGCTTATGGCTTCATCACTGAGGGCCATGAGCGCTTTTCTGAT  
CACTACTATGATACATCATGGAAGCGGCTGATCTTTTACATAAACCATGACTTCAAGCTGGA  
GAGAGAAGTCTGGAAGCGGCTACACGATGAAGGGATAATCCGGCTGTACCAGCGTCCTGGTC  
CCGGAAC TGCCAAAGCCAAGA**CTGA**CCGGGGGCCAGGGCTGCCATGGTCTCCTTGCCTGCTC  
CAAGGCACAGGATACAGTGGGAATCTTGAGACTCTTTGGCCATTTCCCATGGCTCAGACTAA  
GCTCCAAGCCCTTCAGGAGTTCCAAGGGAACACTTGAACCATGGACAAGACTCTCTCAAGAT  
GGCAAATGGCTAATTGAGGTTCTGAAGTTCTTCAGTACATTGCTGTAGGTCTTGAGGCCAGG  
GATTTTTAATTAAATGGGGTGATGGGTGGCCAATACCACAATTCCTGCTGAAAAACACTCTT  
CCAGTCCAAAAGCTTCTTGATACAGAAAAAAGAGCCTGGATTTACAGAAACATATAGATCTG  
GTTTGAATTCCAGATCGAGTTTACAGTTGTGAAATCTTGAAGGTATTACTTAACTTCACTAC  
AGATTGTCTAGAAGACCTTTCTAGGAGTTATCTGATTCTAGAAGGGTCTATACTTGTCTTG  
TCTTTAAGCTATTTGACAACCTCTACGTGTTGTAGAAAACCTGATAATAATACAAATGATTGTT  
GTCCATGGAAAGGCAAATAAATTTTCTACAGTGAAAAA

242/330

**FIGURE 242**

MRSC LWRCRHLSQGVQWSLLLVFLVFFLFALPSFIKEPQTKPSRHQRTENIKERSLQSLAKP  
KSQAPTRARRTTIYAE PAPENNALNTQTQPKAHTTGDRGKEANQAPPEEQDKVPHTAQRAAW  
KSPEKEKTMVNTLS PRGQDAGMASGRTEAQSWKSQDTKTTQGNNGGQTRKLTASRTVSEKHQG  
KAATTAKTLIPKSQHRMLAPTGA VSTRTRQKGVTTAVIPPKEKKPQATPPPAPFQSPTTQRN  
QRLKAANFKSEPRWDFEEKYSFEIGGLQTTCPDSVKIKASKSLWLQKLFLEPNLTLFLDSRHF  
NQSEWDRLEHFAPPPFGFMELNYSLVQKVVTFRFPVPQQQLLLASLPAGSLRCITCAVVGNGG  
ILNNSHMGQEIDSHDYVFRLSGALIKGYEQDVGTRTSFYGFTAFSLTQSLILGNRGFKNVP  
LGKDVRYLHFLEGTRDYEWLEALLMNQTVMSKNLFWFRHRPQEAFREALHMDRYLLLHPDFL  
RYMKNRFLRSKTL DGAHWRIYRPTTGALLLLTALQLCDQVSAYGFITEGHERFSDHYDTSW  
KRLIFYINHDFKLEREVWKRLHDEGIIRLYQRP GPGTAKAKN

**Cytoplasmic Domain:**

amino acids 1-10

**Type II Transmembrane Domain:**

amino acids 11-35

**Lumenal catalytic Domain:**

amino acids 36-600

**Ribonucleotide Reductase small subunit Signature:**

amino acids 481-496

**N-glycosylation Sites:**

amino acids 300-303, 311-314, 331-334, 375-378, 460-463

243/330

**FIGURE 243**

CG**ATG**CGCGGACCCGGGCACCCCCTCCTCCTGGGGCTGCTGCTGGTGCTGGGGCCTTCGCCG  
GAGCAGCGAGTGGAAATTGTTCCCTCGAGATCTGAGGATGAAGGACAAGTTTCTAAAACACCT  
TACAGGCCCTCTTTATTTTAGTCCAAAGTGCAGCAAACACTTCCATAGACTTTATCACAACA  
CCAGAGACTGCACCATTCCCTGCATACTATAAAAGATGCGCCAGGCTTCTTACCCGGCTGGCT  
GTCAGTCCAGTGTGCATGGAGGATAAG**TGA**GCAGACCGTACAGGAGCAGCACACCAGGAGCC  
ATGAGAAGTGCCTTGGAACCAACAGGGAAACAGAACTATCTTTATACACATCCCCTCATGG  
ACAAGAGATTTATTTTGCAGACAGACTCTTCCATAAGTCCTTTGAGTTTTGTATGTTGTTG  
ACAGTTTGCAGATATATATTCGATAAATCAGTGTACTTGACAGTGTTATCTGTCACTTATTT



244/330

**FIGURE 244**

MRGPGHPLLLGLLLVLGPSPEQRVEIVPRDLRMKDKFLKHLTGPLYFSPKCSKHFFHRLYHNT  
RDCTIPAYYKRCARLLTRLAVSPVCMEDK

245/330

**FIGURE 245**

GGGCTGGGCCCCGCCGCAGCTCCAGCTGGCCGGCTTGGTCCTGCGGTCCCTTCTCTGGGAGG  
CCCGACCCCGGCCGCGCCCAGCCCCACC**ATG**CCACCCGCGGGGCTCCGCCGGGCCGCGCCG  
CTCACCGCAATCGCTCTGTTGGTGCTGGGGGCTCCCCTGGTGCTGGCCGGCGAGGACTGCCT  
GTGGTACCTGGACCGGAATGGCTCCTGGCATCCGGGGTTTAACTGCGAGTTCTTCACCTTCT  
GCTGCGGGACCTGCTACCATCGGTACTGCTGCAGGGACCTGACCTTGCTTATCACCGAGAGG  
CAGCAGAAGCACTGCCTGGCCTTCAGCCCCAAGACCATAGCAGGCATCGCCTCAGCTGTGAT  
CCTCTTTGTTGCTGTGGTTGCCACCACCATCTGCTGCTTCCTCTGTTCTGTTGCTACCTGT  
ACCGCCGGCGCCAGCAGCTCCAGAGCCCATTGAAGGCCAGGAGATTCCAATGACAGGCATC  
CCAGTGCAGCCAGTATACCCATACCCCAGGACCCCAAAGCTGGCCCTGCACCCCCACAGCC  
TGGCTTCATGTACCCACCTAGTGGTCCTGCTCCCCAATATCCACTCTACCCAGCTGGGCCCC  
CAGTCTACAACCCTGCAGCTCCTCCTCCCTATATGCCACCACAGCCCTCTTACCCGGGAGCC  
**TGA**GGAACCAGCCATGTCTCTGCTGCCCCCTTCAGTGATGCCAACCTTGGGAGATGCCCTCAT  
CCTGTACCTGCATCTGGTCCTGGGGGTGGCAGGAGTCCTCCAGCCACCAGGCCCCAGACCAA  
GCCAAGCCCTGGGCCCCTACTGGGGACAGAGCCCCAGGGAAGTGGAACAGGAGCTGAACTAGA  
ACTATGAGGGGTTGGGGGGAGGGCTTGGAATTATGGGCTATTTTTTACTGGGGGCAAGGGAGG  
GAGATGACAGCCTGGGTCACAGTGCCTGTTTTCAAATAGTCCCTCTGCTCCCAAGATCCCAG  
CCAGGAAGGCTGGGGCCCTACTGTTTGTCCCCTCTGGGCTGGGGTGGGGGGAGGGAGGAGGT  
TCCGTCAGCAGCTGGCAGTAGCCCTCCTCTCTGGCTGCCCCACTGGCCACATCTCTGGCCTG  
CTAGATTAAAGCTGTAAAGACAAAA

246/330

**FIGURE 246**

MPPAGLRRAAPLTAIALLLVLGAPLVLAGEDCLWYLDNRNGSWHPGFNCEFFTFCCGTCYHRYC  
CRDLTLLITERQQKHCLAFSPKTIAGIASAVILEFVAVVATTICCFLCSCCYLYRRRQQLQSP  
FEGQEIPMTGIPVQPVYPYPQDPKAGPAPPQPGFMYPPSGPAPQYPLYPAGPPVYNPAAPPP  
YMPPQPSYPGA

**Transmembrane Domains:**

amino acids 10-28, 85-110

**N-glycosylation Site:**

amino acids 38-41

**N-myristoylation Sites:**

amino acids 5-10, 88-93

247/330

**FIGURE 247**

GGGGGAGCTAGGCCGGCGGCAGTGGTGGTGGCGGCGGCGCAAGGGTGAGGGCGGCCCCAGAA  
CCCCAGGTAGGTAGAGCAAGAAG**ATGGT**GTTTTCTGCCCTCAAATGGTCCCTTGCAACCATG  
TCATTTCTACTTTCCCTCACTGTTGGCTCTCTTAACTGTGTCCACTCCTTCATGGTGTGAGAG  
CACTGAAGCATCTCCAAAACGTAGTGATGGGACACCATTTCCTTGGAATAAAATACGACTTC  
CTGAGTACGTATCCCAGTTCATTATGATCTCTTGATCCATGCAAACCTTACCACGCTGACC  
TTCTGGGGAACCACGAAAGTAGAAATCACAGCCAGTCAGCCCACCAGCACCATCATCTGCA  
TAGTCACCACCTGCAGATATCTAGGGCCACCCTCAGGAAGGGAGCTGGAGAGAGGCTATCGG  
AAGAACCCCTGCAGGTCTTGGAAACACCCCCCTCAGGAGCAAATTGCACTGCTGGCTCCCGAG  
CCCCCTCTTGTGCGGGCTCCCGTACACAGTTGTCACTTCACTATGCTGGCAATCTTTCGGAGAC  
TTTCCACGGATTTTACAAAAGCACCTACAGAACCAAGGAAGGGGAAGTGGAGATACTAGCAT  
CAACACAATTTGAACCCACTGCAGCTAGAATGGCCTTTCCCTGCTTTGATGAACCTGCCTTC  
AAAGCAAGTTTCTCAATCAAATTAGAAGAGAGCCAAGGCACCTAGCCATCTCCAATATGCC  
ATTGGTGAAATCTGTGACTGTTGCTGAAGGACTCATAGAAGACCATTTTGATGTCACTGTGA  
AGATGAGCACCTATCTGGTGGCCTTCACTATTTAGATTTTGAGTCTGTCAGCAAGATAACC  
AAGAGTGGAGTCAAGGTTTCTGTTTATGCTGTGCCAGACAAGATAAATCAAGCAGATTATGC  
ACTGGATGCTGCGGTGACTCTTCTAGAATTTTATGAGGATTATTTGAGCATAACCGTATCCCC  
TACCCAAACAAGATCTTGCTGCTATTCCCGACTTTCAGTCTGGTGTCTATGGAAAACCTGGGGA  
CTGACAACATATAGAGAATCTGCTCTGTTGTTGATGTCAGAAAAGTCTTCTGCATCAAGTAA  
GCTTGGCATCACAGTGACTGTGGCCCATGAAGTGGCCACCAGTGGTTTGGGAACCTGGTCA  
CTATGGAATGGTGGAAATGATCTTTGGCTAAATGAAGGATTTGCCAAATTTATGGAGTTTGTG  
TCTGTCACTGTGACCCATCCTGAAGTGAAGTTGGAGATTATTTCTTTGGCAAATGTTTTGA  
CGCAATGGAGGTAGATGCTTTAAATTCCTCACACCCTGTGTCTACACCTGTGGAAAATCCTG  
CTCAGATCCGGGAGATGTTTGATGATGTTTCTTATGATAAGGGAGCTTGTATTCTGAATATG  
CTAAGGGAGTATCTTAGCGCTGACGCATTTAAAGTGGTATTGTACAGTATCTCCAGAAGCA  
TAGCTATAAAAAATACAAAAACGAGGACCTGTGGGATAGTATGGCAAGTATTTGCCCTACAG  
ATGGTGTAAAAGGGATGGATGGCTTTTGTCTAGAAAGTCAACATTCATCTTCATCCTCACAT  
TGGCATCAGGAAGGGGTGGATGTGAAAACCATGATGAACACTTGGACACTGCAGAGGGGGTTT  
TCCCCTAATAACCATCACAGTGAGGGGGAGGAATGTACACATGAAGCAAGAGCACTACATGA  
AGGGCTCTGACGGCGCCCCGGACACTGGGTACCTGTGGCATGTTCCATTGACATTATCACC  
AGCAAATCCAACATGGTCCATCGATTTTTTGCTAAAAACAAAAACAGATGTGCTCATCCTCCC  
AGAAGAGGTGGAATGGATCAAATTTAATGTGGGCATGAATGGCTATTACATTGTGCATTACG  
AGGATGATGGATGGGACTCTTTGACTGGCCTTTTAAAGGAACACACACAGCAGTCAGCAGT  
AATGATCGGGCAAGTCTCATTAAACAATGCATTTTCACTCGTCAGCATTTGGGAAGCTGTCCAT  
TGAAAAGGCCTTGGATTTATCCCTGTACTTGAAACATGAAACTGAAATTATGCCCGTGTTTC  
AAGGTTTGAATGAGCTGATTCCCTATGTATAAGTTAATGGAGAAAAGAGATATGAATGAAGTG  
GAAACTCAATTCAAGGCCTTCCTCATCAGGCTGCTAAGGGACCTCATTGATAAGCAGACATG  
GACAGACGAGGGCTCAGTCTCAGAGCAAATGCTGCGGAGTGAACACTACTCTCCTCGCCTGTG  
TGCACAACTATCAGCCGTGCGTACAGAGGGCAGAAGGCTATTTGAGAAAAGTGGAAAGGAATCC  
AATGGAAAACCTTGAGCCTGCCTGTGACGCTGACCTTGGCAGTGTTTGCTGTGGGGGCCAGAG  
CACAGAAGGCTGGGATTTTCTTTATAGTAAATATCAGTTTTCTTTGTCCAGTACTGAGAAAA  
GCCAAATTGAATTTGCCCTCTGCAGAACCCAAAATAAGGAAAAGCTTCAATGGCTACTAGAT  
GAAAGCTTTAAGGGAGATAAAAAATAAAACTCAGGAGTTTCCACAAATCTTACACTCATTGG  
CAGGAACCCAGTAGGATACCCACTGGCCTGGCAATTTCTGAGGAAAAACTGGAACAAACTTG  
TACAAAAGTTTGAACCTTGGCTCATCTTCCATAGCCCACATGGTAATGGGTACAACAAATCAA  
TTCTCCACAAGAACACGGCTTGAAGAGGTAAAAGGATTCTTCAGCTCTTTGAAAGAAAATGG  
TTCTCAGCTCCGTTGTGTCCAACAGACAATTGAAACCATTTGAAGAAAACATCGGTTGGATGG  
ATAAGAATTTTGATAAAATCAGAGTGTGGCTGCAAAGTGAAAAGCTTGAACGTATG**TAAAAA**  
TTCTCCCTTGGCCCGTTCTCTTATCTCTAATCACCACATTTTGTGAGTGTATTTTCAA  
ACTAGAGATGGCTGTTTTGGCTCCAAGTGGAGATCTTTTCCCTTCACTCATTTTGTGA  
CTATCCCTGTGAAAAGAATAGCTGTTAGTTTTTCATGAATGGGCTTTTTTCATGAATGGGCTA  
TCGCTACCATGTGTTTTGTTTCATCACAGGTGTTGCCCTGCAACGTAAACCCAAGTGTTGGGT  
TCCCTGCCACAGAAGAATAAAGTACCTTATTCTCTCAAAAAAAAAAAAAAAAAAAAAAAAAA

248/330

**FIGURE 248**

MVFLPLKWSLATMSFLLSLLALLTVSTPSWCQSTEASPKRSDGTPFPWNKIRLPEYVIPVH  
YDLLIHANLTTLTFWGTTKVEITASQPTSTIILHSHHLQISRATLRKGAGERLSEEPLQVLE  
HPPQEQIALLAPEPLLVLGPYTVVIHYAGNLSETFHGFYKSTYRTKEGELRILASTQFEPTA  
ARMAFPCFDEPAFKASFSIKIRREPRHLAISNMPLVKSVTVAEGLIEDHFDVTVKMSTYLVA  
FIISDFESVSKITKSGVKVSVYAVPDKINQADYALDAAVTLLFYEYDYFSIPYPLPKQDLAA  
IPDFQSGAMENWGLTTYRESALLFDAEKSSASSKLGITVTVAHELAHQWFGNLVTMEWWNDL  
WLNEGFAKFMFVSVSVTHPELKVGDYFFGKCFDAMEVDALNSSHPVSTPVENPAQIREMFD  
DVSYDKGACILNMLREYLSADAFKSGIVQYLQKHSYKNTKNEDLWDSMASICPTDGVKGM DG  
FCRSRQSHSSSSSHWHQEGVDVKTMMNTWTLQRGFPLITITVRGRNVHMKQEHYMKGSDGAPD  
TGYLWHVPLTFITSKSNMVHRFLLKTKTDVLILPEEVEWIKFNVGMNGYYIVHYEDDGWDSL  
TGLLKGTHTAVSSNDRASLINNAFQLV SIGKLSIEKALDLSLYLKHETEIMPVFQGLNELIP  
MYKLMEKRDMNEVETQFKAFILRLRLIDKQTTWTDEGSVSEQMLRSELLLLACVHNYQPCV  
QRAEGYFRKWKESNGNLSLPVDVTLAVFAVGAQSTEGWDFLYSKYQFSLSSTEKSQIEFALC  
RTQNKEKLQWLLDESFKGDKIKTQEFQILTIGRNPVGYPLAWQFLRKNWNKLVQKFELGS  
SSIAHMMVGTTNQFSTRTRLEE VKGFFSSLKENGSQLRCVQQTETIETIENIGWMDKNFDKIR  
VWLQSEKLERM

**Signal peptide:**

amino acids 1-34

**N-glycosylation sites:**

amino acids 70-74, 154-158, 414-418, 760-764, 901-905

**Neutral zinc metallopeptidases, zinc-binding region signature:**

amino acids 350-360

249/330

**FIGURE 249**

CAGCCACAGACGGGTC**ATG**AGCGCGGTATTACTGCTGGCCCTCCTGGGGTTCATCCTCCCAC  
TGCCAGGAGTGCAGGCGCTGCTCTGCCAGTTTGGGACAGTTCAGCATGTGTGGAAGGTGTCC  
GACCTACCCCGGCAATGGACCCCTAAGAACACCAGCTGCGACAGCGGCTTGGGGTGCCAGGA  
CACGTTGATGCTCATTGAGAGCGGACCCCAAGTGAGCCTGGTGCTCTCCAAGGGCTGCACGG  
AGGCCAAGGACCAGGAGCCCCGCGTCACTGAGCACCGGATGGGCCCCGGCCTCTCCCTGATC  
TCCTACACCTTCGTGTGCCGCCAGGAGGACTTCTGCAACAACCTCGTTAACTCCCTCCCGCT  
TTGGGCCCCACAGCCCCCAGCAGACCCAGGATCCTTGAGGTGCCAGTCTGCTTGTCTATGG  
AAGGCTGTCTGGAGGGGACAACAGAAGAGATCTGCCCCAAGGGGACCACACACTGTTATGAT  
GGCCTCCTCAGGCTCAGGGGAGGAGGCATCTTCTCCAATCTGAGAGTCCAGGGATGCATGCC  
CCAGCCAGGTTGCAACCTGCTCAATGGGACACAGGAAATTGGGCCCCGTGGGTATGACTGAGA  
ACTGCAATAGGAAAGATTTTCTGACCTGTATCGGGGGACCACCATTATGACACACGGAAAC  
TTGGCTCAAGAACCCACTGATTGGACCACATCGAATACCGAGATGTGCGAGGTGGGGCAGGT  
GTGTCAGGAGACGCTGCTGCTCATAGATGTAGGACTCACATCAACCTGGTGGGGACAAAAG  
GCTGCAGCACTGTTGGGGCTCAAAATTTCCAGAAGACCACCATCCACTCAGCCCCCTCCTGGG  
GTGCTTGTGGCCTCCTATACCCACTTCTGCTCCTCGGACCTGTGCAATAGTGCCAGCAGCAG  
CAGCGTTCTGCTGAACTCCCTCCCTCCTCAAGCTGCCCCCTGTCCCAGGAGACCGGCAGTGTC  
CTACCTGTGTGCAGCCCCCTTGGAACCTGTTCAAGTGGCTCCCCCGAATGACCTGCCCCAGG  
GGCGCCACTCATTGTTATGATGGGTACATTCATCTCTCAGGAGGTGGGCTGTCCACCAAAT  
GAGCATTACAGGGCTGCGTGGCCCAACCTTCCAGCTTCTTGTGAACCACACCAGACAAATCG  
GGATCTTCTCTGCGCGTGAGAAGCGTGATGTGCAGCCTCCTGCCTCTCAGCATGAGGGAGGT  
GGGGCTGAGGGCCTGGAGTCTCTCACTTGGGGGGTGGGGCTGGCACTGGCCCCAGCGCTGTG  
GTGGGGAGTGGTTTGCCCTTCCTGC**TAA**CTCTATTACCCCCACGATTCTTCACCGCTGCTGA  
CCACCCACACTCAACCTCCCTCTGACCTCATAACCTAATGGCCTTGAGACACCAGATTCTTTC  
CCATTCTGTCCATGAATCATCTTCCCCACACACAATCATTCATATCTACTCACCTAACAGCA  
ACACTGGGGAGAGCCTGGAGCATCCGGACTTGCCCTATGGGAGAGGGGACGCTGGAGGAGTG  
GCTGCATGTATCTGATAATACAGACCCTGTCCTTTCA

250/330

**FIGURE 250**

MSAVLLLALLGFILPLPGVQALLCQFGTVQHVWKVSDLPRQWTPKNTSCDSGLGCQDTLMLI  
ESGPQVSLVLSKGCTEAKDQEPRVTEHRMGPGLSLISYTFVCRQEDFCNNLVNSLPLWAPQP  
PADPGSLRCPVCLSMEGCLEGTTEEICPKGTTTHCYDGLLRRLRGGGIFSNLRVQGCMPQPGCN  
LLNGTQEIGPVGMTENCNRKDFLTCHRGTTIMTHGNLAQEPTDWTTSNTEMCEVGQVCQETL  
LLIDVGLTSTLVGTKGCSTVGAQNSQKTTIHSAPPGVLVASYTHFCSSDLCNSASSSSVLLN  
SLPPQAAPVPGDRQCPTCVQPLGTCSSGSPRMTCPRGATHCYDGYIHLSGGGLSTKMSIQGC  
VAQPSSFLLNHTRQIGIFSAREKRDVQPPASQHEGGGAEGLESLTWGVGLALAPALWWGVVC  
PSC

251/330

**FIGURE 251**

GCGACGGGCAGGACGCCCCGTTCGCCTAGCGCGTGCTCAGGAGTTGGTGTCTGCCTGCGCT  
CAGG**ATG**AGGGGGAATCTGGCCCTGGTGGGCGTTCTAATCAGCCTGGCCTTCCTGTCACTGCTG  
CCATCTGGACATCCTCAGCCGGCTGGCGATGACGCCTGCTCTGTGCAGATCCTCGTCCCTGG  
CCTCAAAGGGGATGCGGGAGAGAAGGGAGACAAAGGCGCCCCGGACGGCCTGGAAGAGTCG  
GCCCCACGGGAGAAAAAGGAGACATGGGGGACAAAGGACAGAAAGGCAGTGTGGGTCTGTCAT  
GGAAAAATTGGTCCCATTGGCTCTAAAGGTGAGAAAGGAGATTCCGGTGACATAGGACCCCC  
TGGTCCTAATGGAGAACCAGGCCTCCCATGTGAGTGCAGCCAGCTGCGCAAGGCCATCGGGG  
AGATGGACAACCAGGTCTCTCAGCTGACCAGCGAGCTCAAGTTCATCAAGAATGCTGTGCGC  
GGTGTGCGCGAGACGGAGAGCAAGATCTACCTGCTGGTGAAGGAGGAGAAGCGCTACGCGGA  
CGCCCAGCTGTCTGCCAGGGCCGCGGGGGCACGCTGAGCATGCCCAAGGACGAGGCTGCCA  
ATGGCCTGATGGCCGCATACCTGGCGCAAGCCGGCCTGGCCCCGTGTCTTCATCGGCATCAAC  
GACCTGGAGAAGGAGGGCGCCTTCGTGTACTCTGACCACTCCCCCATGCGGACCTTCAACAA  
GTGGCGCAGCGGTGAGCCCAACAATGCCTACGACGAGGAGGACTGCGTGGAGATGGTGGCCT  
CGGGCGGCTGGAACGACGTGGCCTGCCACACCACCATGTACTTCATGTGTGAGTTTGACAAG  
GAGAACATG**TGA**GCCTCAGGCTGGGGCTGCCCATTGGGGGCCCCACATGTCCCTGCAGGGTT  
GGCAGGGACAGAGCCCAGACCATGGTGCCAGCCAGGGAGCTGTCCCTCTGTGAAGGGTGGAG  
GCTCACTGAGTAGAGGGCTGTTGTCTAACTGAGAAAATGGCCTATGCTTAAGAGGAAAATG  
AAAGTGTTCCTGGGGTGCTGTCTCTGAAGAAGCAGAGTTTCATTACCTGTATTGTAGCCCCA  
ATGTCATTATGTAATTATTACCCAGAATTGCTCTTCCATAAAGCTTGTGCCTTTGTCCAAGC  
TATACAATAAAATCTTTAAGTAGTGCAGTAGTTAAGTCCAAAAAAAAAAAAAAAAAAAAA



252/330

**FIGURE 252**

MRGNLALVGVLI SLAFLSLLPSGHPQPAGDDACSVQILVPGLKGDAGEKGDKGAPGRPGRVG  
PTGEKGDMDGDKGQKGSVGRHGKIGPIGSKGEKGDSDIGPPGPNGEPGLPCECSQLRKAIGE  
MDNQVSQLTSELKF I KNAVAGVRETESKIYLLVKEEKRYADAQLSCQGRGGTLSMPKDEAAN  
GLMAAYLAQAGLARVFIGINDLEKEGAFVYSDHSPMRTFNKWRSGEPNNAYDEEDCVEMVAS  
GGWNDVACHTTMYFMCEFDKENM

253/330

**FIGURE 253**

AGTGACTGCAGCCTTCCTAGATCCCCTCCACTCGGTTTCTCTCTTTGCAGGAGCACCGGCAG  
CACCAGTGTGTGAGGGGAGCAGGCAGCGGTCCTAGCCAGTTCCTTGATCCTGCCAGACCACC  
CAGCCCCCGGCACAGAGCTGCTCCACAGGCACC**ATG**AGGATCATGCTGCTATTCACAGCCAT  
CCTGGCCTTCAGCCTAGCTCAGAGCTTTGGGGCTGTCTGTAAGGAGCCACAGGAGGAGGTGG  
TTCCTGGCGGGGGCCGCAGCAAGAGGGATCCAGATCTCTACCAGCTGCTCCAGAGACTCTTC  
AAAAGCCACTCATCTCTGGAGGGATTGCTCAAAGCCCTGAGCCAGGCTAGCACAGATCCTAA  
GGAATCAACATCTCCCGAGAAACGTGACATGCATGACTTCTTTGTGGGACTTATGGGCAAGA  
GGAGCGTCCAGCCAGAGGGAAAGACAGGACCTTTCTTACCTTCAGTGAGGGTTCCCTCGGCCC  
CTTCATCCCAATCAGCTTGGATCCACAGGAAAGTCTTCCCTGGGAACAGAGGAGCAGAGACC  
TTT**TAA**GACTCTCCTACGGATGTGAATCAAGAGAACGTCCCCAGCTTTGGCATCCTCAAGT  
ATCCCCCGAGAGCAGAATAGGTACTCCACTTCCGGACTCCTGGACTGCATTAGGAAGACCTC  
TTTCCCTGTCCCAATCCCCAGGTGCGCACGCTCCTGTTACCCTTTCTCTTCCCTGTTCTTGT  
AACATTCTTGTGCTTTGACTCCTTCTCCATCTTTTCTACCTGACCCTGGTGTGGAAACTGCA  
TAGTGAATATCCCCAACCCCAATGGGCATTGACTGTAGAATACCCTAGAGTTCCTGTAGTGT  
CCTACATTAAAAATATAATGTCTCTCTCTATTCCCTCAACAATAAAGGATTTTTGCATATGAA  
AA

254/330

## **FIGURE 254**

MRIMLLFTAILAFSLAQSFQAVCKEPQEEVVPGGGRSKRDPDLYQLLQRLFKSHSSLEGLLK  
ALSQASTDPKESTSPEKRDMDHDFVGLMGKRSVQPEGKTGPFLPSVRVPRPLHPNQLGSTGK  
SSLGTEEQRPL

**Important features:**

**Signal peptide:**

amino acids 1-18

**Tyrosine kinase phosphorylation site.**

amino acids 36-45

**N-myristoylation site.**

amino acids 33-39, 59-65

**Amidation site.**

amino acids 90-94

**Leucine zipper pattern.**

amino acids 43-65

**Tachykinin family signature.**

amino acids 86-92

255/330

**FIGURE 255**

GGGCGTCTCCGGCTGCTCCTATTGAGCTGTCTGCTCGCTGTGCCCCTGTGCCTGCTGTGCC  
CGCGCTGTGCGCGCTGCTACCGCGTCTGCTGGACGCGGGAGACGCCAGCGAGCTGGTGATTG  
GAGCCCTGCGGAGAGCTCAAGCGCCCAGCTCTGCCCCAGGAGCCCAGGCTGCCCCGTGAGTC  
CCATAGTTGCTGCAGGAGTGGAGCC**ATG**AGCTGCGTCCTGGGTGGTGTCAATCCCCCTTGGGGC  
TGCTGTTCCCTGGTCTGCGGATCCCAAGGCTACCTCCTGCCCAACGTCACTCTCTTAGAGGAG  
CTGCTCAGCAAATACCAGCACAAACGAGTCTCACTCCCGGGTCCGCAGAGCCATCCCCAGGGA  
GGACAAGGAGGAGATCCTCATGCTGCACAACAAGCTTCGGGGCCAGGTGCAGCCTCAGGCCT  
CCAACATGGAGTACATGGTGAGCGCCGGCTCCGGCCGCAGAGGCTGGCACCGGGGGTGGGGC  
CTGGGCCACCAGCCTGCTCTGTTCCCCAGCCAGCTCTGTTCCCCAGCCAGTGCGTGTGATGG  
CTGGCTCAGGGTCTCCTCTGGCAGGGGAGGATCCCGGCTCTGTTCTGTTTTGTTTGTGTTGTT  
TTGAGACAGGGTCTCACTCTGCCACTGACGCTGGAGTGCAATGGCACAATCGTCATGCCCTG  
AAACCT**TAG**ACTCCCGGGGTTAAGCGATCCTGCTTCAGCCTCCCAAGTAGCTGGAACTACAG  
GCATGCACCATGGTGCCAGCTAGATTTTAAATATTTTGTGGAGATGGGGGTCTTGCTACGT  
TGCCCAGGCTGGTCTTGAACTCCTAGGCTCAAGCAATCCTCCTGCCTCAGCCTCTCAAAGTG  
CTAGGATTATAGGCATGAGTCACCCTGTCTGGCTCTGGCTCTGTTCTTAACATTCTGCCAAA  
ACAACACACGTGGGTTCCTGTGCAGAGCCTGCCTCGTTGCCTTCATGTCACTCTTGGTAGC  
TCCACTGGGAACACAGCTCTCAGCCTTTCCACCTGGAGGCAGAGTGGGGAGGGGGCCCAGGG  
CTGGGCTTTGCTGATGCTGATCTCAGCTGTGCCACACGCTAGCTGCACCACCCTGACTTCTC  
CTTAGCCCGTGTGAGCCTCACTTTCCACTTGGAGAGTCCTTCCTCGCGTGGTTGCCATGACT  
GTGAGATAAGTCGAGGCTGTGAAGGGCCCGGCACAGACTGACCTGCCTCCCCAACCCCTAGG  
CTTTGCTAACCGGGAAAGGAGCTAACGGTGACAGAAGACAGCCAAGGTCAACCCTCCCGGGT  
GATTGTGATGGGTGTTCCAGGTGTGGTTGGGCGATGCTGCTACTTGACCCCAAGCTCCAGTG  
TGGAACCTTCCTTCCTGGCTGGTTTTCCAGAACTACAGAGGAATGGACCACAGTCTTCCAGG  
GTCCCTCCTCGTCCACCAACCGGGAGCCTCCACCTTGGCCATCCGTCAGCTATGAATGGCTT  
TTTAAACAAACCCACGTCCCAGCCTGGGTAACATGGTAAAGCCCCGTCTCTACAAAAAATC  
CAAGTTAGCCGGGCATGGTGGTGCGCACCTGTAGTCCCAGCTGCAGTGGGACTGAGGTGGAG  
GTGGAGGTGGGGGGTGGGAGCTGAGGAAGGAGGATCGCTTGAGCCTGGGAAGTCGAGGCTGC  
AGTGAGCTGAGATTGCACCACTGCACTCCAGCCTGGGTGACAGAGCAAGACCCTGTCTCAAAAA

256/330

## **FIGURE 256**

MSCVLGGV IPLGLLFLVCGSQGYLLPNVTLLLEELLSKYQHNEHSRVRRAIPREDKEEILML  
HNKLRGQVQPQASNMEYMVSAGSGRRGWHRGWGLGHQPALFPSQLCSPASACDGWLRVSSGR  
GGSRLCSVLFVCFETGSHSATDAGVQWHNRHALKP

**Important features:**

**Signal peptide:**

amino acids 1-22

**N-glycosylation site.**

amino acids 27-31, 41-45

**N-myristoylation site.**

amino acids 126-132, 140-146

**Amidation site.**

amino acids 85-89

257/330

**FIGURE 257**

AAGGAGAGGCCACCGGGACTTCAGTGTCTCCTCCATCCCAGGAGCGCAGTGGCCACT**ATGGG**  
GTCTGGGCTGCCCCCTTGTCTCCTCCTTGACCCTCCTTGGCAGCTCACATGGAACAGGGCCGG  
GTATGACTTTGCAACTGAAGCTGAAGGAGTCTTTTCTGACAAATTCCTCCTATGAGTCCAGC  
TTCCTGGAATTGCTTGAAAAGCTCTGCCTCCTCCTCCATCTCCCTTCAGGGACCAGCGTCAC  
CCTCCACCATGCAAGATCTCAACACCATGTTGTCTGCAACACA**TGA**CAGCCATTGAAGCCTG  
TGTCTTCTTGGCCCGGGCTTTTGGGCCGGGGATGCAGGAGGCAGGCCCCGACCCTGTCTTT  
CAGCAGGCCCCCACCTCCTGAGTGGCAATAAATAAAATTCGGTATGCTG

258/330

**FIGURE 258**

MGSGPLVLLLTLGSSHGTGPGMTLQLKLKESFLTNSSYESSFLELLEKLCLLLHLPSGTS  
VTLHHARSQHHVVCNT

259/330

**FIGURE 259**

AATTGTATCTGTGTAATGTTAAAACAAACGAAATAAAATAGAAGGAAAACTTTCTGAGTTT  
CAAAAACAACAGACTAGTACTCTAAAGAACTCTTTAAAACAATTAAGTGTAGGATTGCAGT  
**TATG**ATTGGATATTATTTAATTCTGTTTCTGATGTGGGGTTCCTCCACTGTGTTCTGTGTGC  
TATTAATATTTACCATTGCAGAAGCTTCATTCAGTGTTGAAAATGAATGCTTAGTGGATCTG  
TGCCTCTTACGCATATGTTACAAATTATCTGGAGTTCCTAATCAATGCAGAGTTCCCTCCC  
CTCCGATTGTTCTAAAT**TAA**ATTGAAAGATGTCTGCTGTGGAAAAAGGCATGTATTTAAATCTG  
TATGATTCTCAACCATCTTTAGTTGGGAAAGGTCCTTGAAAGCCAATGGAAATACTTTTTTT  
TTTTCTTGGCACTAATCAAGTGAGTGTTACCTTTTCACTTAGTAGGATGTGTTGTTACGCTA  
GTAAAATAGAAACCTGTGTTTATTCTCAGGTATTTTAGAAACAACAGCCATCATTTTATTTT  
ATGTGTGTGTTCTTGGCTGTATTCATAAATTATATATTTTGGGCTATCAAATATTACTTCAT  
TCAATATAAATAACAATAGTAGAAGTTGTTTACTTAGATATGCTTTCTAGTTGCATTTTCTC  
AGCCTATGTAAGACTACTTTGTTGTAATAGCCTTTGAAATTTACAGTACTGTCTCTCTACTA  
TCTTCAGATTACTTGATTCAAATAAACCAATTATGTTTGTAATTGATATTAATAAAACCAGA  
ATAAAAGTTCATATCTACCC



260/330

**FIGURE 260**

MIGYYLILFLMWGSSTVFCVLLIFTIAEASFVENECLVDLCLLRICYKLSGVPNQCRVPLP  
SDCSK

**Important features:**

**Signal peptide:**

amino acids 1-29

261/330

**FIGURE 261**

GAGGATTTGCCACAGCAGCGGATAGAGCAGGAGAGCACCACCGGAGCCCTTGAGACATCCTT  
GAGAAGAGCCACAGCATAAGAGACTGCCCTGCTTGGTGTTTTGCAGG**ATG**ATGGTGGCCCTT  
CGAGGAGCTTCTGCATTGCTGGTTCTGTTCCCTTGCACTTTTCTGCCCCCGCCGAGTGATC  
CCAGGACCCAGCCATGGTGCATTACATCTACCAGCGCTTTCGAGTCTTGGAGCAAGGGCTGG  
AAAAATGTACCCAAGCAACGAGGGGCATACATTCAAGAATTCGAAGAGTTCTCAAAAAATATA  
TCTGTCTATGCTGGGAAGATGTCAGACCTACACAAGTGAGTACAAGAGTGCAGTGGGTAACTT  
GGCACTGAGAGTTGAACGTGCCCAACGGGAGATTGACTACATACAATACCTTCGAGAGGCTG  
ACGAGTGCATCGTATCAGAGGACAAGACACTGGCAGAAATGTTGCTCCAAGAAGCTGAAGAA  
GAGAAAAAGATCCGGACTCTGCTGAATGCAAGCTGTGACAACATGCTGATGGGCATAAAGTC  
TTTGAATAAGTGAAGAAGATGATGGACACACATGGCTCTTGGATGAAAGATGCTGTCTATA  
ACTCTCCAAAGGTGTACTTATTAATTGGATCCAGAAACAACACTGTTTGGGAATTTGCAAAC  
ATACGGGCATTCATGGAGGATAACACCAAGCCAGCTCCCCGGAAGCAAATCCTAACACTTTC  
CTGGCAGGGAAACAGGCCAAGTGATCTACAAAGGTTTTCTATTTTTTTCATAACCAAGCAACTT  
CTAATGAGATAATCAAATATAACCTGCAGAAAGAGGACTGTGGAAGATCGAATGCTGCTCCCA  
GGAGGGGTAGGCCGAGCATTGGTTTACCAGCACTCCCCCTCAACTTACATTGACCTGGCTGT  
GGATGAGCATGGGCTCTGGGCCATCCACTCTGGGCCAGGCACCCATAGCCATTGTGTTCTCA  
CAAAGATTGAGCCGGGCACACTGGGAGTGGAGCATTCATGGGATACCCCATGCAGAAGCCAG  
GATGCTGAAGCCTCATTCTCTTGTGTGGGGTTCTCTATGTGGTCTACAGTACTGGGGGCCA  
GGGCCCTCATCGCATCACCTGCATCTATGATCCACTGGGCACTATCAGTGAGGAGGACTTGC  
CCAACTTGTCTTCCCCAAGAGACCAAGAAGTCACTCCATGATCCATTACAACCCAGAGAT  
AAGCAGCTCTATGCCTGGAATGAAGGAAACCAGATCATTACAAACTCCAGACAAAGAGAAA  
GCTGCCTCTGAAG**TAA**TGCATTACAGCTGTGAGAAAGAGCACTGTGGCTTTGGCAGCTGTTC  
TACAGGACAGTGAGGCTATAGCCCCTTCACAATATAGTATCCCTCTAATCACACACAGGAAG  
AGTGTGTAGAAGTGGAATACGTATGCCTCCTTTCCCAAATGTCAGTGCCTTAGGTATCTTC  
CAAGAGCTTAGATGAGAGCATATCATCAGGAAAGTTTCAACAATGTCCATTACTCCCCCAA  
CCTCCTGGCTCTCAAGGATGACCACATTCGTATACAGCCTACTTCAAGCCTTTTGTTTTACT  
GCTCCCCAGCATTTACTGTAACCTGCCATCTTCCCTCCCACAATTAGAGTTGTATGCCAGC  
CCCTAATATTCACCACTGGCTTTTCTCTCCCCTGGCCTTTGCTGAAGCTCTTCCCTCTTTTT  
CAAATGTCTATTGATATTCTCCCATTTTCACTGCCCAACTAAAATACTATTAATATTTCTTT  
CTTTTCTTTTCTTTTTTTTTGAGACAAGGTCTCACTATGTTGCCAGGCTGGTCTCAAACCTCC  
AGAGCTCAAGAGATCCTCCTGCCTCAGCCTCCTAAGTACCTGGGATTACAGGCATGTGCCAC  
CACACCTGGCTTAAAATACTATTTCTTATTGAGGTTTAACTCTATTTCCCTAGCCCTGTC  
CTTCCACTAAGCTTGGTAGATGTAATAATAAAGTGAAAAATATTAACATTTGAATATCGCTTT  
CCAGGTGTGGAGTGTGTCACATCATTGAATTCTCGTTTCACCTTTGTGAAACATGCACAAG  
TCTTTACAGCTGTCATTCTAGAGTTTAGGTGAGTAACACAATTACAAAGTGAAAGATACAGC  
TAGAAAATACTACAAATCCCATAGTTTTTCCATTGCCCAAGGAAGCATCAAATACGTATGTT  
TGTTACCTACTCTTATAGTCAATGCGTTCATCGTTTCAGCCTAAAAATAATAGTCTGTCCC  
TTTAGCCAGTTTTTCATGTCTGCACAAGACCTTTCAATAGGCCTTTCAAATGATAATTCCTCC  
AGAAAACCAGTCTAAGGGTGAGGACCCCAACTCTAGCCTCCTCTTGTCTTGCTGTCTCTGT  
TTCTCTCTTTCTGCTTTAAATTCAATAAAAGTGACACTGAGCAAAAAAAAAAAAAAA

262/330

**FIGURE 262**

MMVALRGASALLVLFLLAAFLPPPQCTQDPAMVHYIYQRFVLEQGLEKCTQATRAYIQEFQE  
FSKNISVMLGRCQTYTSEYKSAVGNLALRVERAQREIDYIQYLREADECIVSEDKTLAEMLL  
QEAEKKKIRTLNLASCDNMLMGIKSLKIVKKMMDTHGSWMKDAVYNPKVYLLIGSRNNTV  
WEFANIRAFMEDNTKPAPRKQILTLWQGTGQVIYKGFLFFHNQATSNEIIKYNLQKRTVED  
RMLLPGGVGRALVYQHSPSTYIDLAVDEHGLWAIHSGPGTHSHLVLTKEPGLGVEHSWDT  
PCRSQDAEASFLLCGVLYVVYSTGGQGPHRITCIYDPLGTISEEDLPNLFFPKRPRSHSMIH  
YNPRDKQLYAWNENQIIYKLQTKRKLPLK

**FIGURE 263**

[illegible]

264/330

**FIGURE 264**

MELSQMSELMGLSVLLGLLALMATAAVARGWLRAGEERSGRPACQKANGFPPDKSSGSKKQK  
QYQIRIRKEKPQQHNFTHRLAAALKSHSGNISCMDFSSNGKYLATCADDRITIRIWSTKDFLQ  
REHRSMRANVELDHATLVRFS PDCRAFI VWLANGDTLRVFKMTKREDGGYTFTATPEDFPKK  
HKAPVIDIGIANTGKFIMTASSD TTVLIWSLKGQVLSTINTNQMNNTAAVSPCGRFVASC  
GFTPDKVWEVCFGKKGEFQEVVRAFELKGHSAAVHSFAFSNDSRRMASVSKDGTWKLWDTDV  
EYKKKQDPYLLKTGRFEEAAGAAPCRLALSPNAQVLALASGSSIHLYNTRRGEKEECFERVH  
GECIANLSFDITGRFLASCGDRAVRLFHNTPGHRAMVEEMQGH LKRASNESTRQRLQQQLTQ  
AQETLKSLGALKK

**Important features:****Signal peptide:**

amino acids 1-25

**N-glycosylation site.**

amino acids 76-80, 92-96, 231-235, 289-293, 378-382, 421-425

**Beta-transducin family Trp-Asp repeat protein.**

amino acids 30-47, 105-118, 107-119, 203-216, 205-217, 296-308

265/330

**FIGURE 265**

TGGCCTCCCCAGCTTGCCAGGCACAAGGCTGAGCGGGAGGAAGCGAGAGGCATCTAAGCAGG  
CAGTGTTTTGCCTTCACCCCAAGTGACCATGAGAGGTGCCACGCGAGTCTCAATCATGCTCC  
TCCTAGTAACTGTGTCTGACTGTGCTGTGATCACAGGGGCCTGTGAGCGGGATGTCCAGTGT  
GGGGCAGGCACCTGCTGTGCCATCAGCCTGTGGCTTCGAGGGCTGCGGATGTGCACCCCGCT  
GGGGCGGGAAGGCGAGGAGTGCCACCCCGGCAGCCACAAGGTCCCCTTCTTCAGGAAACGCA  
AGCACCACACCTGTCCTTGCTTGCCCAACCTGCTGTGCTCCAGGTTCCCGGACGGCAGGTAC  
CGCTGCTCCATGGACTTGAAGAACATCAATTTTTAGGCGCTTGCCCTGGTCTCAGGATACCCA  
CCATCCTTTTCCTGAGCACAGCCTGGATTTTTATTTCTGCCATGAAACCCAGCTCCCATGAC  
TCTCCAGTCCCTACACTGACTACCTGATCTCTCTTGTCTAGTACGCACATATGCACACAG  
GCAGACATACTCCCATCATGACATGGTCCCCAGGCTGGCCTGAGGATGTCACAGCTTGAGG  
CTGTGGTGTGAAAGGTGGCCAGCCTGGTTCTCTTCCCTGCTCAGGCTGCCAGAGAGGTGTA  
AATGGCAGAAAGGACATTCCCCCTCCCCTCCCCAGGTGACCTGCTCTCTTTCCTGGGCCCTG  
CCCCTCTCCCCACATGTATCCCTCGGTCTGAATTAGACATTCTTGGGCACAGGCTCTTGGGT  
GCATTGCTCAGAGTCCCAGGTCCTGGCCTGACCCTCAGGCCCTTCACGTGAGGTCTGTGAGG  
ACCAATTTGTGGGTAGTTCATCTTCCCTCGATTGGTTAACTCCTTAGTTTTAGACCACAGAC  
TCAAGATTGGCTCTTCCCAGAGGGCAGCAGACAGTCACCCCAAGGCAGGTGTAGGGAGCCCA  
GGGAGGCCAATCAGCCCCCTGAAGACTCTGGTCCCAGTCAGCCTGTGGCTTGTGGCCTGTGA  
CCTGTGACCTTCTGCCAGAATTGTCATGCCTCTGAGGCCCTCTTACCACACTTTACCAGT  
TAACCACTGAAGCCCCCAATTCCCACAGCTTTTCCATTAAAATGCAAATGGTGGTGGTTCAA  
TCTAATCTGATATTGACATATTAGAAGGCAATTAGGGTGTTTCCTTAAACAACCTCCTTTCCA  
AGGATCAGCCCTGAGAGCAGGTGGTGACTTTGAGGAGGGCAGTCCTCTGTCCAGATTGGGG  
TGGGAGCAAGGGACAGGGAGCAGGGCAGGGGCTGAAAGGGGCACTGATTACAGACCAGGGAGG  
CAACTACACACCAACATGCTGGCTTTAGAATAAAAGCACCAACTGAAAAA

266/330

## **FIGURE 266**

MRGATRVSIMLLLVTVSDCAVITGACERDVQCGAGTCCAISLWLRGLRMCTPLGREGEETCHP  
GSHKVPFFFRKRKHHTCPCLPNLLCSRFPDGRYRCSMDLKNINF

**Signal peptide:**

amino acids 1-19

**Tyrosine kinase phosphorylation site:**

amino acids 88-95

**N-myristoylation sites:**

amino acids 33-39, 35-41, 46-52

267/330

**FIGURE 267**

AGCGCCCGGGCGTCGGGGCGGTAAAAGGCCGGCAGAAGGGAGGCACTTGAGAAATGTCTTTC  
CTCCAGGACCCAAGTTTCTTCACCATGGGGATGTGGTCCATTGGTGCAGGAGCCCTGGGGGC  
TGCTGCCTTGGCATTGCTGCTTGCCAACACAGACGTGTTTCTGTCCAAGCCCCAGAAAGCGG  
CCCTGGAGTACCTGGAGGATATAGACCTGAAAACACTGGAGAAGGAACCAAGGACTTTCAAA  
GCAAAGGAGCTATGGGAAAAAAATGGAGCTGTGATTATGGCCGTGCGGAGGCCAGGCTGTTT  
CCTCTGTGCGAGAGGAAGCTGCGGATCTGTCCTCCCTGAAAAGCATGTTGGACCAGCTGGGCG  
TCCCCCTCTATGCAGTGGTAAAGGAGCACATCAGGACTGAAGTGAAGGATTTCCAGCCTTAT  
TTCAAAGGAGAAATCTTCCTGGATGAAAAGAAAAAGTTCTATGGTCCACAAAGGCGGAAGAT  
GATGTTTATGGGATTTATCCGTCTGGGAGTGTGGTACAACCTTCTTCCGAGCCTGGAACGGAG  
GCTTCTCTGGAAACCTGGAAGGAGAAGGCTTCATCCTTGGGGGAGTTTTCGTGGTGGGATCA  
GGAAAGCAGGGCATTTCTTCTTGAGCACCGAGAAAAAGAATTTGGAGACAAAGTAAACCTACT  
TTCTGTTCTGGAAGCTGCTAAGATGATCAAACCACAGACTTTGGCCTCAGAGAAAAAATGAT  
TGTGTGAAACTGCCCAGCTCAGGGATAACCAGGGACATTCACCTGTGTTTCATGGGATGTATT  
GTTTCCACTCGTGTCCCTAAGGAGTGAGAAACCCATTTATACTCTACTCTCAGTATGGATTA  
TTAATGTATTTTAATATTCTGTTTAGGCCCACTAAGGCAAAATAGCCCCAAAACAAGACTGA  
CAAAAATCTGAAAAACTAATGAGGATTATTAAGCTAAAACCTGGGAAATAGGAGGCTTAAAA  
TTGACTGCCAGGCTGGGTGCAGTGGCTCACACCTGTAATCCCAGCACTTTGGGAGGCCAAGG  
TGAGCAAGTCACTTGAGGTCGGGAGTTCGAGACCAGCCTGAGCAACATGGCGAAACCCCGTC  
TCTACTAAAAATACAAAATCACCCGGGTGTGGTGGCAGGCACCTGTAGTCCCAGCTACCCG  
GGAGGCTGAGGCAGGAGAATCACTTGAACCTGGGAGGTGGAGGTTGCGGTGAGCTGAGATCA  
CACCCTGTATTCCAGCCTGGGTGACTGAGACTCTAACTAA



268/330

**FIGURE 268**

MSFLQDPSFFTGMWSIGAGALGAAALALLANTDVFLSKPQKALEYLEDIDLKTLEKEPR  
TFKAKELWEKNGAVIMAVRRPGCFLCREEAADLSSLKSMLDQLGVPLYAVVKEHIRTEVKDF  
QPYFKGEIFLDEKKKFYGPQRRKMMFMGFIRLGVWYNFFRAWNGGFSGNLEGEFGFILGGVFV  
VGSGKQGILLEHREKEFGDKVNLLSVLEAAKMIKPQTLASEKK

269/330

**FIGURE 269**

ACGGACCGAGGGTTCGAGGGAGGGACACGGACCAGGAACCTGAGCTAGGTCAAAGACGCCCCG  
GGCCAGGTGCCCCGTGCGAGGTGCCCCTGGCCGGAGATGCGGTAGGAGGGGCGAGCGCGAGA  
AGCCCCTTCCTCGGCGCTGCCAACCCGCCACCCAGCCC**ATG**GC GAACCCCGGGCTGGGGCTG  
CTTCTGGCGCTGGGCCTGCCGTTCTTGCTGGCCCGCTGGGGCCGAGCCTGGGGGCAAATACA  
GACCACTTCTGCAAATGAGAATAGCACTGTTTTGCCTTCATCCACCAGCTCCAGCTCCGATG  
GCAACCTGCGTCCGGAAGCCATCACTGCTATCATCGTGGTCTTCTCCCTCTTGGCTGCCTTG  
CTCCTGGCTGTGGGGCTGGCACTGTTGGTGCGGAAGCTTCGGGAGAAGCGGCAGACGGAGGG  
CACCTACCGGCCCAGTAGCGAGGAGCAGTTCTCCCATGCAGCCGAGGCCCGGGCCCCCTCAGG  
ACTCCAAGGAGACGGTGCAGGGCTGCCTGCCCATC**TAG**GTCCCCTCTCCTGCATCTGTCTCC  
CTTCATTGCTGTGTGACCTTGGGGAAAGGCAGTGCCCTCTCTGGGCAGTCAGATCCACCCAG  
TGCTTAATAGCAGGGAAGAAGGTACTTCAAAGACTCTGCCCCTGAGGTCAAGAGAGGATGGG  
GCTATTCACCTTTTATATATTTATATAAAATTAGTAGTGAGATGTAAAAAAAAAAAAAAAAAAAA

270/330

**FIGURE 270**

MANPGLGLLLALGLPFLLARWGRAWGQIQTTSANENSTVLPSTSSSSDGNLRPEAITAIIV  
VFSLLAALLLAVGLALLVRKLREKRQTEGTYRPSSEEQFSHAAEARAPQDSKETVQGCLPI

271/330

**FIGURE 271**

AATATATCATCTATTTATCATTAATCAATAATGTATTCTTTTATTCCAATAACATTTGGGTT  
TTGGGATTTTAAATTTTCAAACACAGCAGAAATGACATTTTTTCTGTCACTATTATTATTGTTG  
GTATGTGAAGCTATTTGGAGATCCAATTCAGGAAGCAACACATTGGAGAATGGCTACTTTCT  
ATCAAGAAATAAAGAGAACCACAGTCAACCCACACAATCATCTTTAGAAGACAGTGTGACTC  
CTACCAAAGCTGTCAAAACCACAGGCAAGGGCATAGTTAAAGGACGGAATCTTGACTCAAGA  
GGGTTAATTCTTGGTGCTGAAGCCTGGGGCAGGGGTGTAAAGAAAAACACTTAGATTCAATG  
ATTGTAAATTTAAGGCAAATACACATATTAGTATTACCTTAGTGTAATGTATCCCTGTCATA  
TATACAATAAGGTGAAATTATAAGTACCCTATGCAGTTGGCTGGACAGTTCTAAATTGGACT  
TTATTAATTTTTTAAATCAGTAACTGATTTATCACTGGCTATGTGCTTAGATCTACAGGAGA  
TCATATAATTTGATACAAATAAAAGAAAAGTGTCTCTCCCCTTACAGAATTGACATTTTAA  
ATGCGATACAGTTAGAATAGGAAATATGACATTAGAAAGGAAGAATGACAGGGAGAAAGGAA  
AGAAGGGAAAATGTTGCCAAGGAAAAAAAAA

272/330

**FIGURE 272**

MTFFLSLLLLLVCEAIWRSNSGSNTLENGYFLSRNKENHSQPTQSSLEDSVTPTKAVKTTGK  
GIVKGRNLDSRGLILGAEAWGRGVKKNT

**FIGURE 273**

GCCAGGAAATAACTAGAGAGGAAACA**ATG**GGGTTATTTCAGAGGTTTTGTTTTCTCTTAGTTCT  
 GTGCCTGCTGCACCAGTCAAATACTTCTTCATTAAAGCTGAATAATAATGGCTTTGAAGGATA  
 TTGTCATTGTTATAGATCCTAGTGTGCCAGAAGATGAAAAAATAATTGAACAAATAGAGGAT  
 ATGGTGACTACAGCTTCTACGTACCTGTTTGAAGCCACAGAAAAAAGATTTTTTTTCAAAAA  
 TGTATCTATATTAATTCTCTGAGAAATTGGAAGGAAAAATCCTCAGTACAAAAGGCCAAAAATG  
 AAAACCATAAACATGCTGATGTTATAGTTGCACCACCTACACTCCCAGGTAGAGATGAACCA  
 TACACCAAGCAGTTTCACAGAATGTGGAGAGAAAAGCGAATACATTCACTTCACCCCGTACCT  
 TCTACTTTGGAAAAAAACAAAAATGAATATGGACCACCAGGCAAACCTGTTTGCTCATGAGTGGG  
 CTCACCTCCGGTGGGGAGTGTTGTAGTAGTACAATGAAGATCAGCCTTTCTACCGTGCTAAG  
 TCAAAAAAAATCGAAGCAACAAGGTGTTCCGCAGGTATCTCTGGTAGAAATAGAGTTTATAA  
 GTGTCAAGGAGGCAGCTGTCTTAGTAGAGCATGCAGAATTGATTCTACAACAAAACCTGTATG  
 GAAAAGATTGTCAATTCTTTCTGATAAAAGTACAAACAGAAAAAGCATCCATAATGTTTATG  
 CAAAGTATTGATTCTGTTGTTGAATTTTGTAAACGAAAAAACCCATAATCAAGAAGCTCCAAG  
 CCTACAAAACATAAAGTGCAATTTTGAAGTACATGGGAGGTGATTAGCAATTTCTGAGGATT  
 TTA AAAACACCATAACCCATGGTGACACCACCTCCTCCACCTGTCTTCTCATTGCTGAAGATC  
 AGTCAAAGAATTGTGTGCTTAGTTCTTGATAAGTCTGGAAGCATGGGGGGTAAGGACCGCCT  
 AAATCGAATGAATCAAGCAGCAAAAACATTTCTGCTGCAAGACTGTTGAAAATGGATCCTGGG  
 TGGGGATGGTTCACCTTTGATAGTACTGCCACTATTGTAAATAAGCTAATCCAAATAAAAAAGC  
 AGTGATGAAAGAAACACACTCATGGCAGGATTACCTACATATCCTCTGGGAGGAACCTCCAT  
 CTGCTCTGGAATTAATATGCATTTCAAGGTGATTGGAGAGCTACATTCCCAACTCGATGGAT  
 CCGAAGTACTGCTGCTGACTGATGGGGAGGATAACACTGCAAGTTCTTGTATTGATGAAGTG  
 AAACAAAGTGGGGCCATTGTTCAATTTTATGCTTTTGGGAAGAGCTGCTGATGAAGCAGTAAT  
 AGAGATGAGCAAGATAACAGGAGGAAGTCAATTTTATGTTTCAGATGAAGCTCAGAACAAATG  
 GCCTCATTGATGCTTTTGGGGCTCTTACATCAGGAAATACTGATCTCTCCAGAAAGTCCCTT  
 CAGCTCGAAAGTAAGGGATTAACACTGAATAGTAATGCCTGGATGAACGACACTGTCATAAT  
 TGATAGTACAGTGGGAAAGGACACGTTCTTTCTCATCACATGGAACAGTCTGCCTCCAGTA  
 TTTCTCTCTGGGATCCCACTGGAACAATAATGGAAAATTTCAAGTGGATGCAACTTCCAAA  
 ATGGCTATCTCAGTATTCCAGGAAGTGCAAAAGTGGGCACTGGGCATACAATCTTCAAGC  
 CAAAGCGAAACCCAGAAACATTAACATATTACAGTAACCTCTCGAGCAGCAAATTTCTTCTGTGC  
 CTCCAATCACAGTGAATGCTAAAATGAATAAGGACGTAAACAGTTTCCCCAGCCCCAATGATT  
 GTTTACGCAGAAATTTCTACAAGGATATGTACCTGTTCTTGGAGCCAATGTGACTGCTTTCAT  
 TGAATCACAGAAATGGACATACAGAAGTTTGGAACTTTTGGATAATGGTGCAAGGCGTGATT  
 CTTTCAAGAATGATGGAGTCTACTCTCAGGTATTTTACAGCATATACAGAAAATGGCAGATAT  
 AGCTTAAAAGTTTCGGGCTCATGGAGGAGCAAACACTGCCAGGCTAAAATTTACGGCCTCCACT  
 GAATAGAGCCGCGTACATAACCAGGCTGGGTAGTGAACGGGGAAATTTGAAGCAAACCCGCCAA  
 GACCTGAAATTGATGAGGATACTCAGACCACCTTGGAGGATTTACAGCCGAACAGCATCCGGA  
 GGTGCATTTGTGGTATCACAAGTCCCAAGCCTTCCCTTGCTGACCAATACCCACCAAGTCA  
 AATCACAGACCTTGATGCCACAGTTCATGAGGATAAGATTATTTCTACATGGACAGCACGAG  
 GAGATAATTTTGATGTTGGAAAAGTTCAACGTTATATCATAAGAATAAGTGCAAGTATTCTT  
 GATCTAAGAGACAGTTTTTGATGATGCTCTTCAAGTAAATACTACTGATCTGTCACCAAAGGA  
 GGCCAACTCCAAGGAAAGCTTTGCATTTAAACCAGAAAAATATCTCAGAAGAAAAATGCAACCC  
 ACATATTTATTGCCATTAAAAGATAGATAAAAAGCAATTTGACATCAAAAGTATCCAAACATT  
 GCACAAGTAACCTTTGTTTTATCCCTCAAGCAAATCCTGATGACATTGATCCTACACCTACTCC  
 TACTCCTACTCCTACTCCTGATAAAAGTCATAATTTCTGGAGTTAATATTTCTACGCTGGTAT  
 TGTCTGTGATTGGGTCTGTTGTAATTGTTAACTTTATTTTAAAGTACCACCATT**TGA**ACCTTA  
 ACGAAGAAAAAAATCTTCAAGTAGACCTAGAAGAGAGTTTTTAAAAAACAAAACAAATGTAAGT  
 AAAGGATATTTCTGAATCTTAAATTCATCCCATGTGTGATCATAAATCATATAAAATAATT  
 TTAAGATGTCGGAAGGATACCTTTGATTAATAAAAAACACTCATGGATATGTAAAAACTGT  
 CAAGATTAAAAATTTAATAGTTTTCATTTATTTGTTATTTTATTTGTAAGAAATAGTGATGAAC  
 AAAGATCCTTTTTTCATACTGATACCTGGTGTATATTATTTGATGCAACAGTTTTCTGAAAT  
 GATATTTCAAATTGATCAAGAAATTAATAATCATCTATCTGAGTAGTCAAAATACAAGTAA  
 GGAGAGCAAAATAAACAACTTTGGAAAAAAATAAAAAAAATGAAAAAATGAAAAAATGAAAAA  
 AAAAAAATAAAAAAATAAAAAAATAAAAAAATAAAAAAATAAAAAAATAAAAAAATAAAAAA  
 AAAAAAATAAAAAAATAAAAAAATAAAAAAATAAAAAAATAAAAAAATAAAAAAATAAAAAA

274/330

**FIGURE 274**

MGLFRGFVFLLVLCLLHQSNSTSFIKLNNNGFEDIVIVIDPSVPEDEKIIIEQIEDMVTASTY  
LFEATEKRFFFKNVSILIPENWKENPQYKRPKHENHKKHADVIVAPPTLPGRDEPYTKQFTEC  
GEKGEYIHFTPDLLLGGKKQNEYGPPGKLFVHEWAHLRWGVFDEYNEDQPFYRAKSKKIEATR  
CSAGISGRNRVYKCQGGSCLSRACRIDSTTKLYGKDCQFFPDKVQTEKASIMFMQSIDSVVE  
FCNEKTHNQEAPSLQNIKCENFRSTWEVISNSEDFKNTIPMVTPPPPPVFSLLKISQRIVCLV  
LDKSGSMGGKDRLNRMNQAAKHFLQTVENGSWVGMVHFDSTATIVNKLIQIKSSDERNTLM  
AGLPTYPLGGTSICSGIKYAFQVIGELHSQLDGSEVLLLTGDEDNTASSCIDEVKQSGAIVH  
FIALGRAADEAVIEMSKITGGSHFYVSDEAQNNGLIDAFGALTSGNTDLSQKSLQLESKGLT  
LNSNAWMNDTVIIDSTVGKDTFFLITWNSLPPSISLWDPSGTIMENFTVDATSKMAYLSIPG  
TAKVGTWAYNLQAKANPETLTITVTSRAANSSVPPITVNAKMNDVNSFPSPMIVYAEILQG  
YVPVLGANVTAFIESQNGHTEVLELLDNGAGADSFKNDGVYSRYFTAYTENGRYSLKVBRAHG  
GANTARLKLRPPLNRAAYIPGWVVNGEIEANPPRPEIDEDTQTTLEDFSRASGGAFVVSQV  
PSLPLPDQYPPSQITDLDATVHEDKIILTWTAPGDNFDVGKVQRYIIRISASILDLRDSFDD  
ALQVNTTDLSPKEANSKESFAFKPENISEENATHIFIAIKSIDKSNLTSKVSNIAQVTLFIP  
QANPDDIDPTPTPTPTPTPDKSHNSGVNISTLVLSVIGSVVIVNFILSTTI

**Signal peptide:**

amino acids 1-21

**Putative transmembrane domains:**

amino acids 284-300, 617-633

**Leucine zipper pattern.**

amino acids 469-491, 476-498

**N-glycosylation site.**amino acids 20-24, 75-79, 340-344, 504-508, 542-546, 588-592,  
628-632, 811-815, 832-836, 837-841, 852-856, 896-900

275/330

**FIGURE 275**

CTCCTTAGGTGGAAACCCTGGGAGTAGAGTACTGACAGCAAAGACCGGGAAAGACCATACGTCCCCG  
GGCAGGGGTGACAACAGGTGTCTCTTTTGTATCTCGTGTGTGGCTGCCTTCCTATTTCAAGGAAAG  
ACGCCAAGGTAAATTTTGACCCAGAGGAGCAATGATGTAGCCACCTCCTAACCTTCCCTTCTTGAACC  
CCCAGTTATGCCAGGATTTACTAGAGAGTGTCAACTCAACCAGCAAGCGGCTCCTTCGGCTTAACCTT  
GTGGTTGGAGGAGAGAACCCTTGTGGGGCTGCGTTCTCTTAGCAGTGCTCAGAAAGTGAAGTTCGCTGA  
GGGTGGACCAGAAGAAAGGAAAGGTCCCCCTCTTGCTGTTGGCTGCACATCAGGAAGGCTGTGATGGG  
AATGAAGGTGAAAACCTTGAGATTTTCACTTTCAGTTCATTGCTTCTGCCTGCAAGATCATCCTTTAAAA  
GTAGAGAAGCTGCTCTGTGTGGTGGTTAACTCCAAGAGGCAGAACTCGTTCTAGAAGGAAATGGATG  
CAAGCAGCTCCGGGGGGCCCCAAACGCATGCTTCCTGTGGTCTAGCCCAGGGAAGCCCTTCCGTGGGG  
GCCCCGGCTTTGAGGGATGCCACCGGTTCTGGACGCATGGCTGATTCTGAATGATGATGGTTCGCC  
GGGGGCTGCTTGCGTGGATTTCCCGGGTGTGGTTTGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGT  
CCTGTACATGTTGGCCTGCACCCCAAAAGGTGACGAGGAGCAGCTGGCACTGCCCAGGGCCAACAGC  
CCCACGGGGAAGGAGGGGTACCAGGCCGTCTTCAGGAGTGGGAGGAGCAGCACCAGCAACTACGTGA  
GCAGCCTGAAGCGGCAGATCGCACAGCTCAAGGAGGAGCTGCAGGAGAGGAGTGAGCAGCTCAGGAG  
TGGGCAGTACCAAGCCAGCGATGCTGCTGGCTGGCTGGGCTGGGACAGGAGCCCCCAGAGAAAAACCCAG  
GCCGACCTCCTGGCCTTCTGCACTCGCAGGTGGACAAGGCAGAGGTGAATGCTGGCGTCAAGCTGG  
CCACAGAGTATGCAGCAGTGCTTTTCGATAGCTTTACTCTACAGAAGGTGTACCAGCTGGAGAGCTGG  
CCTTACCCGCCACCCCGAGGAGAAGCCTGTGAGGAAGGACAAGCGGGATGAGTTGGTGGAAAGCCATT  
GAATCAGCCTTGAGAGACCTGAACAATCTGCAGAGAACAGCCCAATCACCCTCCTTACACGGCCT  
CTGATTTTCATAGAAGGGATCTACCGAACAGAAAGGGACAAAGGGACATTGTATGAGCTCACCTTCAA  
AGGGGACCACAAACACGAATTCAAACGGCTCATCTTATTTTCGACCATTCAGCCCCATCATGAAAGTG  
AAAAATGAAAGCTCAACATGGCCAAACACGCTTATCAATGTTATCGTGCCTTAGCAAAAAAGGGTGG  
ACAAGTTCCGGCAGTTTCATGCAGAATTTCAAGGAGATGTGCATTGAGCAGGATGGGAGAGTCCATCT  
CACTGTTGTTTACTTTGGGAAAGAAGAAATAAATGAAGTCAAAGGAATACTTGAAAACACTTCCAAA  
GCTGCCAACTTCAGGAACCTTACCTTCATCCAGCTGAATGGAGAATTTTCTCGGGGAAAGGGACTTG  
ATGTTGGAGCCCGCTTCTGGAAGGGAAGCAACGTCCTTCTCTTTTCTGTGATGTGGACATCTACTT  
CACATCTGAATTCCTCAATACGTGTAGGCTGAATACACAGCCAGGGAAGAAGGTATTTTATCCAGTT  
CTTTTCAGTCAGTACAATCCTGGCATAATATACGGCCACCATGATGCAGTCCCTCCCTTGGAAACAGC  
AGCTGGTCATAAAGAAGGAAACTGGATTTTGGAGAGACTTTGGATTTGGGATGACGTGTCTAGTATCG  
GTACAGACTTCATCAATATAGGTGGGTTTGATCTGGACATCAAAGGCTGGGGCGGAGAGGATGTGCAC  
CTTTATCGCAAGTATCTCCACAGCAACCTCATAGTGGTACGGACGCTGTGCGAGGACTCTTCCACC  
TCTGGCATGAGAAGCGCTGCATGGACGAGCTGACCCCCGAGCAGTACAAGATGTGCATGCAGTCCAA  
GGCCATGAACGAGGCATCCACGGCCAGCTGGGCATGCTGGTGTTCAGGCACGAGATAGAGGCTCAC  
TCTCGCAAACAGAAACAGAAAGACAAGTGAACAAAAAACAATGAATCCCAGAGAAGGATTTGTGGGAGA  
CACTTTTTCTTTCTTTTGTCAATTACTGAAAGTGGCTGCAACAGAGAAAAGACTTCCATAAAGGACG  
ACAAAAGAATTGGACTGATGGGTGAGAGATGAGAAAAGCCTCCGATTTCTCTCTGTGGGCTTTTAC  
AACAGAAATCAAAATCTCCGCTTTGCCTGCAAAAGTAACCCAGTTGCACCCTGTGAAGTGTCTGACA  
AAGGCAGAATGCTTGTGAGATTATAAGCCTAATGGTGTGGAGGTTTTTGATGGTGTGTACAAATCACT  
GAGACCTGTTGTTTTGTGTGCTCATTGAAATATTCATGATTTAAGAGCAGTTTTGTAAAAAATTCAT  
TAGCATGAAAGGCAAGCATATTTCTCCTCATATGAATGAGCCTATCAGCAGGGCTCTAGTTTCTAGG  
AATGCTAAAATATCAGAAGGCAGGAGAGGAGATAGGCTTATTATGATACTAGTGAGTACATTAAGTA  
AAATAAAATGGACCAGAAAAGAAAAGAACCATAAATATCGTGTATATTTTCCCCAAGATTAACCA  
AAAATAATCTGCTTATCTTTTGGTTGTCCTTTTAACTGTCTCCGTTTTTTTCTTTTATTTAAAAAT  
GCACTTTTTTTCCCTTGTGAGTTATAGTCTGCTTATTTAATTACCACTTTGCAAGCCTTACAAGAGA  
GCACAAGTTGGCCTACATTTTATATTTTTTAAAGAGATACTTTGAGATGCATTATGAGAACTTTCA  
GTTCAAAGCATCAAAATGATGCCATATCCAAGGACATGCCAAATGCTGATTCTGTGAGGCACTGAAT  
GTCAGGCATTGAGACATAGGGAAGGAATGTTTTGTACTAATACAGACGTACAGATACTTTCTCTGAA  
GAGTATTTTGAAGAGGAGCAACTGAACACTGGAGGAAAAGAAAATGACACTTTCTGCTTTACAGAA  
AAGGAAACTCATTACAGACTGGTGATATCGTGATGTACCTAAAAGTCAGAAACCACATTTTCTCCTCA  
GAAGTAGGGACCGCTTTCTTACCTGTTTAAATAAACCAGTATACCGTGTGAACCAACAATCTCT  
TTTCAAAACAGGGTGCTCCTCCTGGCTTCTGGCTTCCATAAGAAGAAATGGAGAAAAATATATATAT  
ATATATATATATTGTGAAAGATCAATCCATCTGCCAGAATCTAGTGGGATGGAAGTTTGTCTACAT  
GTTATCCACCCAGCCAGGTGGAAGTAACTGAATATTTTTTAAATTAAGCAGTTTACTCAATCA  
CCAAGATGCTTCTGAAAATTGCATTTTATTACCATTTCAAACATTTTTTTAAAAATAAATACAGTTA  
ACATAGAGTGGTTTTCTTCATTCATGTGAAAATTATTAGCCAGCACCAGATGCATGAGCTAATTATCT  
CTTTGAGTCCTTGCTTCTGTTTGTCTCAGTAACTCATTGTTTAAAGCTTCAAGAACATTCAAGC  
TGTTGGTGTGTTAAAAAATGCATTGTATTGTTTGTAGTTTATGAAATTTAATTTAAACAC  
AGGCCATGAATGGAAGGTGGTATTGCACAGCTAATAAATATGATTGTGGATATGAA



276/330

**FIGURE 276**

MMVRRGLLAWISRVVLLVLLCCAISVLYMLACTPKGDEEQLALPRANSPTGKEGYQAVLQ  
EWEEQHRNYVSSLKRQIAQLKEELQERSEQLRNGQYQASDAAGLGLDRSPPEKTQADLLAFL  
HSQVDKAEVNAGVKLATEYAAVPFDSFTLQKVYQLETGLTRHPPEKPVRKDKRDELVEAIES  
ALETINNPAENSPNHRPYTASDFIEGIYRTERDKGTLYELTFKGDHKHEFKRLILFRPFSP  
MKVKNEKLNMANNTLINVIVPLAKRVDKFRQFMQNFREMCIEQDGRVHLLTVVYFGKEEINEVK  
GILENTSKAANFRNFTFIQLNGEFSRGKGLDVGARFWKGSNVLLFFCDVDIYFTSEFLNTCR  
LNTQPGKKVFYPVLFSQYNPGIIYGHHDVPPLEQQLVIKKETGFWRDFGFGMTCQYRSDFI  
NIGGFDLDIKGWGGEDVHLYRKYLHSNLIVVRTPVRGLFHLWHEKRCMDELTPEQYKMCMQS  
KAMNEASHGQLGMLVFRHEIEAHLRKQKQKTSSKKT

277/330

**FIGURE 277**

GAAAGA**ATG**TTGTGGCTGCTCTTTTTTCTGGTGACTGCCATTCATGCTGAACTCTGTCAACC  
AGGTGCAGAAAATGCTTTTAAAGTGAGACTTAGTATCAGAACAGCTCTGGGAGATAAAGCAT  
ATGCCTGGGATACCAATGAAGAATACCTCTTCAAAGCGATGGTAGCTTTCTCCATGAGAAAA  
GTTCCCAACAGAGAAGCAACAGAAATTTCCCATGTCCTACTTTGCAATGTAACCCAGAGGGT  
ATCATTCTGGTTTGTGGTTACAGACCCTTCAAAAAATCACACCCTTCCTGCTGTTGAGGTGC  
AATCAGCCATAAGAATGAAACAAGAACCGGATCAACAATGCCTTCTTTCTAAATGACCAAAC  
CTGGAATTTTTTAAAAATCCCTTCCACACTTGCACCACCCATGGACCCATCTGTGCCCATCTG  
GATTATTATATTTGGTGTGATATTTTGCATCATCATAGTTGCAATTGCACTACTGATTTTAT  
CAGGGATCTGGCAACGTAGAAGAAAGAACAAAGAACCATCTGAAGTGGATGACGCTGAAGAT  
AAGTGTGAAAACATGATCACAATTGAAAATGGCATCCCCTCTGATCCCCTGGACATGAAGGG  
GGGCATATTAATGATGCCTTCA**TGA**CAGAGGATGAGAGGGCTCACCCCTCTCTGAAGGGCTGT  
TGTTCTGCTTCCTCAAGAAATTAAACATTTGTTTCTGTGTGACTGCTGAGCATCCTGAAATA  
CCAAGAGCAGATCATATATTTTGTTCACCATTCTTCTTTTGTAATAAATTTTGAATGTGCT  
TGAAAGTGAAAAGCAATCAATTATACCCACCAACACCACTGAAATCATAAGCTATTCACGAC  
TCAAAATATTCTAAAATATTTTTCTGACAGTATAGTGTATAAATGTGGTCATGTGGTATTTG  
TAGTTATTGATTTAAGCATTTTTAGAAATAAGATCAGGCATATGTATATATTTTCACTTC  
AAAGACCTAAGGAAAAATAAATTTTCCAGTGGAGAATACATATAATATGGTGTAGAAATCAT  
TGAAAATGGATCCTTTTTTGACGATCACTTATATCACTCTGTATATGACTAAGTAAACAAAAG  
TGAGAAGTAATTATTGTAAATGGATGGATAAAAATGGAATTACTCATATACAGGGTGGAATT  
TTATCCTGTTATCACACCAACAGTTGATTATATATTTTCTGAATATCAGCCCCTAATAGGAC  
AATTCTATTTGTTGACCATTTCTACAATTTGTAAAAGTCCAATCTGTGCTAACTTAATAAAG  
TAATAATCATCTCTTTTTTAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

278/330

**FIGURE 278**

MLWLLFFLVTAIHAELCQPGAENAFKVRLSIRTALGDKAYAWDTNEEYLFKAMVAFSMRKVP  
NREATEISHVLLCNVTQRVSFVFWVTDPSKNHTLPAVEVQSAIRMNKNRINNAFFLNDQTL  
FLKIPSTLAPPMDPSVPIWIIIFGVIFCIIIVAIALLILSGIWQRRRKNKEPSEVDDAEDKC  
ENMITIENGIPSDPLDMKGGILMMPS

279/330

**FIGURE 279**

AACTCAAACCTCCTCTCTCTGGGAAAACGCGGTGCTTGCTCCTCCCGGAGTGGCCTTGGCAGG  
GTGTTGGAGCCCTCGGTCTGCCCCGTCCGGTCTCTGGGGCCAAGGCTGGGTTTCCCTC**ATGT**  
ATGGCAAGAGCTCTACTCGTGCGGTGCTTCTTCTCCTTGGCATAACAGCTCACAGCTCTTTGG  
CCTATAGCAGCTGTGGAAATTTATACCTCCCGGGTGCTGGAGGCTGTTAATGGGACAGATGC  
TCGGTTAAAATGCACTTTCTCCAGCTTTGCCCTGTGGGTGATGCTCTAACAGTGACCTGGA  
ATTTTCGTCCTCTAGACGGGGGACCTGAGCAGTTTGTATTCTACTACCACATAGATCCCTTC  
CAACCCATGAGTGGGCGGTTTAAGGACCGGGTGTCTTGGGATGGGAATCCTGAGCGGTACGA  
TGCCTCCATCCTTCTCTGGAAACTGCAGTTCGACGACAATGGGACATACACCTGCCAGGTGA  
AGAACCCACCTGATGTTGATGGGGTGATAGGGGAGATCCGGCTCAGCGTCGTGCACACTGTA  
CGCTTCTCTGAGATCCACTTCCTGGCTCTGGCCATTGGCTCTGCCTGTGCACTGATGATCAT  
AATAGTAATTGTAGTGGTCCTCTTCCAGCATTACCGGAAAAAGCGATGGGCCGAAAGAGCTC  
ATAAAGTGGTGGAGATAAAATCAAAGAAGAGGAAAGGCTCAACCAAGAGAAAAAGGTCTCT  
GTTTATTTAGAAAGACACAGAC**TAA**CAATTTTAGATGGAAGCTGAGATGATTTCCAAGAACAA  
GAACCCTAGTATTTCTTGAAGTTAATGGAACTTTTCTTTGGCTTTTCCAGTTGTGACCCGT  
TTTCCAACCAGTTCTGCAGCATATTAGATTCTAGACAAGCAACACCCCTCTGGAGCCAGCAC  
AGTGCTCCTCCATATCACAGTCATACACAGCCTCATTATTAAGGTCTTATTTAATTTTCA  
GTGTAAATTTTTTCAAGTGCTCATTAGGTTTTATAACAAGAAGCTACATTTTTTGCCCTTAA  
GACACTACTTACAGTGTTATGACTTGTATACACATATATTGGTATCAAAGGGGATAAAAGCC  
AATTTGTCTGTTACATTTCTTTTACGTATTTCTTTTAGCAGCACTTCTGCTACTAAAGTTA  
ATGTGTTTACTCTCTTTCTTCCCACATTCTCAATTAAAAGGTGAGCTAAGCCTCCTCGGTG  
TTTCTGATTAACAGTAAATCCTAAATTCAAAGTTAAATGACATTTTTATTTTTATGTCTC  
TCCTTAACTATGAGACACATCTTGTTTTACTGAATTTCTTTCAATATTCAGGTGATAGATT  
TTTGTCG

280/330

**FIGURE 280**

MYGKSSTRAVLLLLGIQLTALWPAAVEIYTSRVLEAVNGTDARLKCTFSSFAPVGDALTVT  
WNFRPLDGGPEQFVFYYHIDPFQPMSGRFKDRVSWDGNPERYDASILLWKLQFDDNGTYTCQ  
VKNPPDVDGVIGEIRLSVVHTVRFSEIHFLALAIGSACALMIIIVIVVVL FQHYRKKRWAER  
AHKVVEIKSKEEERLNQEKKVSVYLEDTD

281/330

**FIGURE 281**

GCATTTTTGTCTGTGCTCCCTGATCTTCAGGTCACCACC**ATGA**AAGTTCTTAGCAGTCCTGGT  
ACTCTTGGGAGTTTCCATCTTTCTGGTCTCTGCCCAGAATCCGACAACAGCTGCTCCAGCTG  
ACACGTATCCAGCTACTGGTCCTGCTGATGATGAAGCCCCTGATGCTGAAACCACTGCTGCT  
GCAACCACTGCGACCACTGCTGCTCCTACCACTGCAACCACCGCTGCTTCTACCACTGCTCG  
TAAAGACATTCCAGTTTTACCCAAATGGGTTGGGGATCTCCCGAATGGTAGAGTGTGTCCCT**T**  
**GAG**ATGGAATCAGCTTGAGTCTTCTGCAATTGGTCACAACATTCATGCTTCCTGTGATTTC  
ATCCAACCTACTTACCTTGCCTACGATATCCCCTTTATCTCTAATCAGTTTATTTTCTTTCAA  
ATAAAAAATAACTATGAGCAACATAAAAAAAAAAAAAA

282/330

**FIGURE 282**

MKFLAVLVLLGVSI FLVSAQNPTTAAPADTYPATGPADDEAPDAETTAAATTATTAAPTAT  
TAASTTARKDIPVLPKWVGDL PNGRVCP

283/330

**FIGURE 283**

GGACTCTGAAGGTCCCAAGCAGCTGCTGAGGCCCCCAAGGAAGTGGTTCCAACCTTGGACCC  
CTAGGGGTCTGGATTTGCTGGTTAACAAGATAACCTGAGGGCAGGACCCCATAGGGGA**ATGC**  
TACCTCCTGCCCTTCCACCTGCCCTGGTGTTCACGGTGGCCTGGTCCCTCCTTGCCGAGAGA  
GTGTCCTGGGTCAGGGACGCAGAGGACGCTCACAGACTCCAGCCCTTTGTTACCGAGAGGAC  
ACTTGGCAAGGTCCAGCGATGGTCCGGAGTCCACACACAGACTGGCGGCAGGGCAGGAGGGG  
GACAGTTCTGTTGTGCTTGGTTGGACAGTAAGAGGGTCTTGCCAGTCCAGGGTGGGGGGCG  
GCAAACCTCCATAAAGAACCAGAGGGTCTGGGCCCCGGCCACAGAGTCATCTGCCCAGCTCCT  
CTGCTGCTGGCCAGTGGGAGTGGCACGAGGTGGGGCTTTGTGCCAG**TAA**AACCACAGGCTGG  
ATTTGCCTGCGGGCCATGGTCCCTGTCTAGGGCAGCAATTCTCAACCTTCTTGCTCTCAGGA  
CCCCAAAGAGCTTTCATTGTATCTATTGATTTTTTACCACATTAGCAATTAAACTGAGAAAT  
GGGCCGGGCACGGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGTGGAT  
CACCTGAGATCAGGAGTTCAAGACCAGCCTGGCCAACATGGTGAAACCTTGTCTACTAAAAA  
TACAAAAAATTAGCCAGGCACAGTGGTGTGCACTGGTAGTCCCAGTTACTCGGGAGGCTGAG  
GCAGGAAAATCGCTTGAACCCAGGAGGCGGACGTTGCGGTGAGCCGAGATCGCGCCGCTGAT  
TCCAGCCTGGGCGACAAGAGTGAGACTCCATCTCACACA



284/330

**FIGURE 284**

MLPPALPPALVFTVAWSLLAERVSWSVRDAEDAHRLQPFVTERTLGKVQRWSGVHTQTGGRAG  
GGQFCCAWLDSKRVLASPGWGAANSIKNQRVWAPATESSAQLCCWPVGVARGGALCQ

285/330

**FIGURE 285**

GTC**ATG**CCAGTGCCTGCTCTGTGCCTGCTCTGGGCCCTGGCAATGGTGACCCGGCCTGCCTCA  
GCGGCCCCCATGGGCGGCCCAGAACTGGCACAGCATGAGGAGCTGACCCTGCTCTTCCATGG  
GACCCTGCAGCTGGGCCAGGCCCTCAACGGTGTGTACAGGACCACGGAGGGACGGCTGACAA  
AGGCCAGGAACAGCCTGGGTCTCTATGGCCGCACAATAGAACTCCTGGGGCAGGAGGTCAGC  
CGGGGCCGGGATGCAGCCCAGGAACTTCGGGCAAGCCTGTTGGAGACTCAGATGGAGGAGGA  
TATTCTGCAGCTGCAGGCAGAGGCCACAGCTGAGGTGCTGGGGGAGGTGGCCCAGGCACAGA  
AGGTGCTACGGGACAGCGTGCAGCGGCTAGAAGTCCAGCTGAGGAGCGCCTGGCTGGGCCCT  
GCCTACCGAGAATTTGAGGTCTTAAAGGCTCACGCTGACAAGCAGAGCCACATCCTATGGGC  
CCTCACAGGCCACGTGCAGCGGCAGAGGCGGGAGATGGTGGCACAGCAGCATCGGCTGCGAC  
AGATCCAGGAGAGACTCCACACAGCGGCGCTCCCAGCC**TGA**ATCTGCCTGGATGGAAGTGA  
GACCAATCATGCTGCAAGGAACACTTCCACGCCCCGTGAGGCCCTGTGCAGGGAGGAGCTG  
CCTGTTCACCTGGGATCAGCCAGGGCGCCGGGCCCCACTTCTGAGCACAGAGCAGAGACAGAC  
GCAGGCGGGGACAAAGGCAGAGGATGTAGCCCCATTGGGGAGGGGTGGAGGAAGGACATGTA  
CCCTTTCATGCCTACACACCCCTCATTAAGCAGAGTCGTGGCATTTCAAAAAAAAAAAAAA  
AAAAAAAAAAAAAAAAAAAAAAAAA

286/330

**FIGURE 286**

MPVPALCLLWALAMVTRPASAAPMGGPELAQHEELTLLFHGTLQLGQALNGVYRTTEGRLTK  
ARNSLGLYGRTIELLGQEVSRGRDAAQELRASLLETQMEEDILQLQAEATAEVLGEVAQAQK  
VLRDSVQRLEVQLRSAWLGPAYREFEVLKAHADKQSHILWALTGHVQRQRREMVAQQHRLRQ  
IQERLHTAALPA

287/330

**FIGURE 287**

GGCAAC**ATG**GCTCAGCAGGCTTGCCCCAGAGCCATGGCAAAGAATGGACTTGTAATTTGCAT  
CCTGGTGATCACCTTACTCCTGGACCAGACCACCAGCCACACATCCAGATTAAAAGCCAGGA  
AGCACAGCAAACGTCGAGTGAGAGACAAGGATGGAGATCTGAAGACTCAAATTGAAAAGCTC  
TGGACAGAAGTCAATGCCTTGAAGGAAATTCAAGCCCTGCAGACAGTCTGTCTCCGAGGCAC  
TAAAGTTCACAAGAAATGCTACCTTGCTTCAGAAGGTTTGAAGCATTTCCATGAGGCCAATG  
AAGACTGCATTTCCAAAGGAGGAATCCTGGTTATCCCCAGGAACTCCGACGAAATCAACGCC  
CTCCAAGACTATGGTAAAAGGAGCCTGCCAGGTGTCAATGACTTTTGGCTGGGCATCAATGA  
CATGGTCACGGAAGGCAAGTTTGTGACGTCAACGGAATCGCTATCTCCTTCCTCAACTGGG  
ACCGTGCACAGCCTAACGGTGGCAAGCGAGAAAACGTGTCTCCTGTTCTCCAATCAGCTCAG  
GGCAAGTGGAGTGATGAGGCCTGTGCGCAGCAGCAAGAGATACATATGCGAGTTCACCATCCC  
TAA**ATAG**GTCTTTCTCCAATGTGTCTCCTCAAGCAAGATTCATCATAACTTATAGGTTTCATGA  
TCTCTAAGATCAAGTAAAAATCATAATTTTTACTTATTAAAAAATTGCAACACAAGATCAAT  
GTCCATAGCAATATGATAGCATCAGCCAATTTTGCTAACACATTTCTTTGGGATTTTGCCCT  
TCCTGGGGTATAGGGGATCAGAAATATTGATCCATGTGCACGCAGATAAAATGGCTTCTGCT  
AAACAGACTAAATCTTTCTCTCTAGTCTTTCTCACTTGTACAAACCCAGTTTGTTCATCAA  
AAATCACAGTAGCAATGCAACTCATCACTCTAGAAAAGCAAGCTTAGGCTACCTGAAAGATT  
TTCCCTTGGAAGTTTAGCGTATGTTTGACTAACAAAAATTCCTTACATCAGAGACTCTAGGT  
GCTATATAATCCAAAACTTTTCAGCCTGTTGCTCATTCTGTCCCATGCTGGCAATAATACC  
TTGTCAGCCCATTACCCTTATTTTGAATTGCTCCATCTCCTGGTGGGACTTGTATCTTGTCT  
GCCATATCAGAACACAAACCCCTGAAGAGGTTCTGATTTGATTTTTTTTTTTCTTCATGCC  
TACCCTTTTTTTGGAAGTTTCCAGCCGCAATTTGAAATGAAATGACAAGGTGTATATTTGAT  
CAATTTTCATTCCCACCATTGCATTACAACCTCTAACTTAAATGGGTAACCTAAGGCATAT  
CAAAGAAGCAGATTGCATGATAAACGGAAATAGAAAAAAGAACCTACATTTATTTTGCTTT  
AGCATCCTTACTCTCACCTTTTATGAGATTGAGAGTGGACTTACATTTCTTTTTTACATTT  
TCGTATATTTATTTTTTTTAGCCATCATTATATGTTTAAGTCTATTATGGGCAACCAATCTT  
TGGAAGCTGAAAACCTGAATTTAAAGAATGCTATCTTGGAATTTGCATACGTCTGTGCAATT  
TTTTATTCTGCCTAGTGCTATTCTGCTTGTTTAACTAGATTGTACAAAATAACTTCATTGCT  
TAATATCAAATTACAAAGTTTAGACTTGGAGGGAAATGGGCTTTTTTAGAAGCAAACAATTTT  
AAATATATTTTGTCTTCAAATAAATAGTGTTTAAACATTGAATGTGTTTTGTGAACAATAT  
CCCACTTTGCAAACCTTAACTACACATGCTTGGAATTAAGTTTTAGCTGTTTTTCATTGCTCA  
ATAATAAAGCCTGAATTCTGATCAATAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

288/330

**FIGURE 288**

MAQQACPRAMAKNGLVICILVITLLLDQTTSHTSRLKARKHSKRRVRDKDGD LKTQIEKLWT  
EVNALKEIQALQTVCLRGTKVHKKCYLASEGLKHFHEANEDCISKGGILVIPRNSDEINALQ  
DYGKRSLPGVNDFWLGINDMVTEGKFVDVNGIAISFLNWDRAQPNGGKRENCVLFSQSAQ GK  
WSDEACRSSKRYICEFTIPK

289/330

**FIGURE 289**

GCGAGGACCGGGTATAAGAAGCCTCGTGCCCTTGCCCGGGCAGCCGCAGGTTCCCCGCGCGC  
CCCGAGCCCCCGCGCC**ATGA**AAGCTCGCCGCCCTCCTGGGGCTCTGCGTGGCCCTGTCCTGCA  
GCTCCGCTGCTGCTTTCTTAGTGGGCTCGGCCAAGCCTGTGGCCCAGCCTGTCGCTGCGCTG  
GAGTCGGCGGCGGAGGCCGGGGCCGGGACCCTGGCCAACCCCTCGGCACCCTCAACCCGCT  
GAAGCTCCTGCTGAGCAGCCTGGGCATCCCCGTGAACCACCTCATAGAGGGCTCCCAGAAGT  
GTGTGGCTGAGCTGGGTCCCCAGGCCGTGGGGGCCGTGAAGGCCCTGAAGGCCCTGCTGGGG  
GCCCTGACAGTGTTTGGCT**TGA**AGCCGAGACTGGAGCATCTACACCTGAGGACAAGACGCTGCC  
CACCCGCGAGGGCTGAAAACCCCGCCGCGGGGAGGACCGTCCATCCCCTTCCCCCGGCCCT  
CTCAATAAACGTGGTTAAGAGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA  
AAAAAAAAAAAA

290/330

**FIGURE 290**

MKLAALLGLCVALSCSSAAAFVLGSAKPVAQPVAALESAAEAGAGTLANPLGTINPLKLLLS  
SLGIPVNHLEGSQKCVAELGPQAVGAVKALKALLGALTVFG

291/330

**FIGURE 291**

TGAAGGACTTTTCCAGGACCCCAAGGCCACACACTGGAAGTCTTGCAGCTGAAGGGAGGCACT  
CCTTGGCCTCCGCAGCCGATCAC**ATGA**AAGGTGGTGCCAAGTCTCCTGCTCTCCGTCCTCCTG  
GCACAGGTGTGGCTGGTACCCGGCTTGGCCCCCAGTCCTCAGTCGCCAGAGACCCAGCCCC  
TCAGAACCAGACCAGCAGGGTAGTGCAGGCTCCCAGGGAGGAAGAGGAAGATGAGCAGGAGG  
CCAGCGAGGAGAAGGCCGGTGAGGAAGAGAAAGCCTGGCTGATGGCCAGCAGGCAGCAGCTT  
GCCAAGGAGACTTCAAACCTTCGATTTCAGCCTGCTGCGAAAGATCTCCATGAGGCACGATGG  
CAACATGGTCTTCTCTCCATTTGGCATGTCCTTGGCCATGACAGGCTTGATGCTGGGGGCCA  
CAGGGCCGACTGAAACCCAGATCAAGAGAGGGCTCCACTTGCAGGCCCTGAAGCCCACCAAG  
CCCGGGCTCCTGCCTTCCCTCTTTAAGGGACTCAGAGAGACCCTCTCCCGCAACCTGGAACCT  
GGGCCTCTCACAGGGGAGTTTTGCCTTCATCCACAAGGATTTTGATGTCAAAGAGACTTTCT  
TCAATTTATCCAAGAGGTATTTTGATACAGAGTGCCTGCTATGAATTTTCGCAATGCCTCA  
CAGGCCAAAAGGCTCATGAATCATTACATTAACAAAGAGACTCGGGGGAAAATTCCCAAACCT  
GTTTGATGAGATTAATCCTGAAACCAAATTAATTCTTGTGGATTACATCTTGTTCAAAGGGA  
AATGGTTGACCCCATTTGACCCTGTCTTCACCGAAGTCGACACTTTCCACCTGGACAAGTAC  
AAGACCATTAAGGTGCCCATGATGTACGGTGCAGGCAAGTTTGCCTCCACCTTTGACAAGAA  
TTTTCGTTGTCATGTCCTCAAACCTGCCCTACCAAGGAAATGCCACCATGCTGGTGGTCCTCA  
TGGAGAAAATGGGTGACCACCTCGCCCTTGAAGACTACCTGACCACAGACTTGGTGGAGACA  
TGGCTCAGAAACATGAAAACCAGAAACATGGAAGTTTTCTTTCCGAAGTTCAAGCTAGATCA  
GAAGTATGAGATGCATGAGCTGCTTAGGCAGATGGGAATCAGAAGAATCTTCTCACCCCTTG  
CTGACCTTAGTGAACCTCTCAGCTACTGGAAGAAATCTCCAAGTATCCAGGGTTTTACGAAGA  
ACAGTGATTGAAGTTGATGAAAGGGGCACTGAGGCAGTGGCAGGAATCTTGTCAGAAATTAC  
TGCTTATTCCATGCCTCCTGTCATCAAAGTGGACCGGCCATTTTCATTTTCATGATCTATGAAG  
AAACCTCTGGAATGCTTCTGTTTTCTGGGCAGGGTGGTGAATCCGACTCTCCTAT**TAA**ATTCAGG  
ACATGCATAAGCACTTCGTGCTGTAGTAGATGCTGAATCTGAGGTATCAAACACACACAGGA  
TACCAGCAATGGATGGCAGGGGAGAGTGTTCCTTTTGTTCTTAAGTATAGTTTAGGGTGTTCTC  
AAATAAATACAGTAGTCCCCACTTATCTGAGGGGGATACATTCAAAGACCCCCAGCAGATGC  
CTGAAACGGTGGACAGTGCTGAACCTTATATATATTTTTTCTTACACATACATACCTATGAT  
AAAGTTTAATTTATAAATTAGGCACAGTAAGAGATTAACAATAATAACAACATTAAGTAAAA  
TGAGTTACTTGAACGCAAGCACTGCAATACCATAACAGTCAAACCTGATTATAGAGAAGGCTA  
CTAAGTGACTCATGGGCGAGGAGCATAGACAGTGTGGAGACATTGGGCAAGGGGAGAATTCA  
CATCCTGGGTGGGACAGAGCAGGACGATGCAAGATTCCATCCCACTACTCAGAATGGCATGC  
TGCTTAAGACTTTTAGATTGTTTATTTCTGGAATTTTTTCATTTAATGTTTTTGGACCATGGT  
TGACCATGGTTAACTGAGACTGCAGAAAGCAAAACCATGGATAAGGGAGGACTACTACAAAA  
GCATTAAATTGATACATATTTTTTAAAAA



292/330

**FIGURE 292**

MKVVPSLLLSVLLAQVWLVPGLAPSPQSPETPAPQNQTSRVVQAPREEEDEQEASEEKAGE  
EEKAWLMASRQQLAKETSNFGFSLLRKISMRHDGNMVFSPFGMSLAMTGLMLGATGPTETQI  
KRGLHLQALKPTKPGLLPSLFKGLRETLSRNLELGLSQGSFAFIHKDFDVKETFFNLSKRYF  
DTECVPMNFRNASQAKRLMNHYINKETRGKIPKLFDEINPETKLILVDYILFKGKWLTTFDP  
VFTEVDTFHLDKYKTIKVPMMYGAGKFASTFDKNFRCHVLKLPYQGNATMLVVLMEKMGDHL  
ALEDYLTDLVETWLRNMKTRNMEVFFPKFKLDQKYEMHELLRQMGIRRIFFPFADLSELSA  
TGRNLQVSRVLRRTVIEVDERGTEAVAGILSEITAYSMPPVIKVDRPFHFMIYEETSGMLLF  
LGRVVNPTLL

293/330

**FIGURE 293**

CTGGGATCAGCCACTGCAGCTCCCTGAGCACTCTCTACAGAGACGCGGACCCCAGAC**ATG**AG  
GAGGCTCCTCCTGGTCACCAGCCTGGTGGTTGTGCTGCTGTGGGAGGCAGGTGCAGTCCCAG  
CACCCAAGGTCCCTATCAAGATGCAAGTCAAACACTGGCCCTCAGAGCAGGACCCAGAGAAG  
GCCTGGGGCGCCCGTGTGGTGGAGCCTCCGGAGAAGGACGACCAGCTGGTGGTGTCTGTTCCC  
TGTCCAGAAGCCGAAACTCTTGACCACCGAGGAGAAGCCACGAGGTGAGGGCAGGGGCCCCA  
TCCTTCCAGGCACCAAGGCCTGGATGGAGACCGAGGACACCCTGGGCCGTGTCCTGAGTCCC  
GAGCCCGACCATGACAGCCTGTACCACCCTCCGCCTGAGGAGGACCAGGGCGAGGAGAGGCC  
CCGGTTGTGGGTGATGCCAAATCACCAGGTGCTCCTGGGACCGGAGGAAGACCAAGACCACA  
TCTACCACCCCCAG**TAG**GGCTCCAGGGGCCATCACTGCCCCCGCCCTGTCCCAAGGGCCAGG  
CTGTTGGGACTGGGACCCTCCCTACCCTGCCCCAGCTAGACAAATAAACCCCAGCAGGCAAA  
AAAAAAAAAAAAAAAAA

294/330

**FIGURE 294**

MRRLLLVTSLVVVLLWEAGAVPAPKVPIKMQVKHWPSEQDPEKAWGARVVEPPEKDDQLVVL  
FPVQKPKLLTTEEKPRGQGRGPILPGTKAWMETEDTLGRVLSPEPDHDSLYHPPPEEDQGEE  
RPRLWVMPNHQVLLGPEEDQDHIYHPQ

295/330

**FIGURE 295**

AGAAAGCTGCACTCTGTTGAGCTCCAGGGCGCAGTGGAGGGAGGGAGTGAAGGAGCTCTCTG  
TACCCAAGGAAAGTGCAGCTGAGACTCAGACAAGATTACA**ATGA**ACCAACTCAGCTTCCTGC  
TGTTTCTCATAGCGACCACCAGAGGATGGAGTACAGATGAGGCTAATACTTACTTCAAGGAA  
TGGACCTGTTCTTCGTCTCCATCTCTGCCCAGAAGCTGCAAGGAAATCAAAGACGAATGTCC  
TAGTGCATTTGATGGCCTGTATTTTCTCCGCACTGAGAATGGTGTTATCTACCAGACCTTCT  
GTGACATGACCTCTGGGGGTGGCGGCTGGACCCTGGTGGCCAGCGTG CATGAGAATGACATG  
CGTGGGAAGTGCACGGTGGGCGATCGCTGGTCCAGTCAGCAGGGCAGCAAAGCAGACTACCC  
AGAGGGGGACGGCAACTGGGCCAACTACAACACCTTTGGATCTGCAGAGGCGGCCACGAGCG  
ATGACTACAAGAACCCTGGCTACTACGACATCCAGGCCAAGGACCTGGGCATCTGGCACGTG  
CCCAATAAGTCCCCCATGCAGCACTGGAGAAACAGCTCCCTGCTGAGGTACCGCACGGACAC  
TGGCTTCCTCCAGACACTGGGACATAATCTGTTTGGCATCTACCAGAAATATCCAGTGAAAT  
ATGGAGAAGGAAAGTGTTGGACTGACAACGGCCCCGGTGATCCCTGTGGTCTATGATTTTGGC  
GACGCCCAGAAAACAGCATCTTATTACTCACCTATGGCCAGCGGGAATTCACTGCGGGATT  
TGTT CAGTTCAGGGTATTTAATAACGAGAGAGCAGCCAACGCCTTGTGTGCTGGAATGAGGG  
TCACCGGATGTAACACTGAGCATCACTGCATTGGTGGAGGAGGATACTTTCCAGAGGCCAGT  
CCCCAGCAGTGTGGAGATTTTTCTGGTTTTGATTGGAGTGGATATGGAACCTCATGTTGGTTA  
CAGCAGCAGCCGTGAGATAACTGAGGCAGCTGTGCTTCTATTCTATCGT**TGA**GAGTTTTGTG  
GGAGGGAACCCAGACCTCTCCTCCCAACCATGAGATCCCAAGGATGGAGAACAACCTTACCCA  
GTAGCTAGAATGTTAATGGCAGAAGAGAAAACAATAAATCATATTGACTCAAGAAAAAAA

296/330

**FIGURE 296**

MNQLSFLLFLIATTRGWSTDEANTYFKEWTCSSSPSLPRSCKEIKDECPSAFDGLYFLRTEN  
GVIYQTFCDMTSGGGGWTLVASVHENDMRGKCTVGDRWSSQQGSKADYPEGDGNWANYNTFG  
SAEAATSDDYKNPGYYDIQAKDLGIWHVPNKSPMQHWRNSSLLRYRTDTGFLQTLGHNLFGI  
YQKYPVKYGEKGCWTDNGPVIPVVYDFGDAQKTASYYSPTYGQREFTAGFVQFRVFNNERAAN  
ALCAGMRVTGCNTEHHCIGGGGYFPEASPPQCGDFSGFDWSGYGTHVGYSSSREITEAAVLL  
FYR

297/330

**FIGURE 297**

GCGGAGCCGGCGCCGGCTGCGCAGAGGAGCCGCTCTCGCCGCCGCCACCTCGGCTGGGAGCC  
CACGAGGCTGCCGCATCCTGCCCTCGGAACAATGGGACTCGGCGCGCGAGGTGCTTGGGCCG  
CGCTGCTCCTGGGGACGCTGCAGGTGCTAGCGCTGCTGGGGGCCGCCCATGAAAGCGCAGCC  
ATGGCGGCATCTGCAAACATAGAGAATTCTGGGCTTCCACACAACCTCCAGTGCTAACTCAAC  
AGAGACTCTCCAACATGTGCCTTCTGACCATACAAATGAACTTCCAACAGTACTGTGAAAC  
CACCAACTTCAGTTGCCTCAGACTCCAGTAATACAACGGTCACCACCATGAAACCTACAGCG  
GCATCTAATAACAACACCAGGGATGGTCTCAACAAATATGACTTCTACCACCTTAAAGTC  
TACACCCAAAACAACAAGTGTTTCACAGAACACATCTCAGATATCAACATCCACAATGACCG  
TAACCCACAATAGTTCAAGTGACATCTGCTGCTTCATCAGTAACAATCACAACAACCTATGCAT  
TCTGAAGCAAAGAAAGGATCAAAATTTGATACTGGGAGCTTTGTTGGTGGTATTGTATTAAC  
GCTGGGAGTTTTATCTATTCTTTACATTGGATGCAAATGTATTACTCAAGAAGAGGCATTC  
GGTATCGAACCATAGATGAACATGATGCCATCATTTAAGGAAATCCATGGACCAAGGATGGA  
ATACAGATTGATGCTGCCCTATCAATTAATTTTGGTTTATTAATAGTTTAAAACAATATTCT  
CTTTTTGAAAATAGTATAAACAGGCCATGCATATAATGTACAGTGTATTACGTAAATATGTA  
AAGATTCTTCAAGGTAACAAGGGTTTGGGTTTTGAAATAAACATCTGGATCTTATAGACCGT  
TCATACAATGGTTTTAGCAAGTTCATAGTAAGACAAACAAGTCCTATCTTTTTTTTTTTGGCT  
GGGGTGGGGGCATTGGTCACATATGACCAGTAATTGAAAGACGTCATCACTGAAAGACAGAA  
TGCCATCTGGGCATACAAATAAGAAGTTTGTACAGCACTCAGGATTTTGGGTATCTTTTGT  
AGCTCACATAAAGAACTTCAGTGCTTTTCAGAGCTGGATATATCTTAATTACTAATGCCACA  
CAGAAATTATACAATCAAACCTAGATCTGAAGCATAATTTAAGAAAAACATCAACATTTTTTG  
TGCTTTAAACTGTAGTAGTTGGTCTAGAAACAAAATACTCC

298/330

**FIGURE 298**

MGLGARGAWAALLLGTLQVLALLGAAHESAAMAASANIENSGLPHNSSANSTETLQHVP  
SDH  
TNETSNSTVKPPTSVASDSSNTTVTTMKPTAASNTTTPGMVSTNMTSTTLKSTPKTTSV  
SQN  
TSQISTSTMTVTHNSSVTSAASSVTITTTMHSEAKKGSKFDTGSFVGGIVLTLGVLSI  
LYIG  
CKMYYSRRGIRYRTIDEHDAII

299/330

**FIGURE 299**

CAGCCGGGTCCCAAGCCTGTGCCTGAGCCTGAGCCTGAGCCTGAGCCCGAGCCGGGAGCCGG  
TCGCGGGGGCTCCGGGCTGTGGGACCGCTGGGCCCCCAGCG**ATG**GCGACCCTGTGGGGAGGC  
CTTCTTCGGCTTGGCTCCTTGCTCAGCCTGTCGTGCCTGGCGCTTTCGCTGCTGCTGCTGGC  
GCAGCTGTCAGACGCCGCCAAGAATTCGAGGATGTCAGATGTAAATGTATCTGCCCTCCCT  
ATAAAGAAAATTCTGGGCATATTTATAATAAGAACATATCTCAGAAAGATTGTGATTGCCTT  
CATGTTGTGGAGCCCATGCCTGTGCGGGGGCCTGATGTAGAAGCATACTGTCTACGCTGTGA  
ATGCAAATATGAAGAAAGAAGCTCTGTCACAATCAAGGTACCATTATAATTTATCTCTCCA  
TTTTGGGCCTTCTACTTCTGTACATGGTATATCTTACTCTGGTTGAGCCCATACTGAAGAGG  
CGCCTCTTTGGACATGCACAGTTGATACAGAGTGATGATGATATTGGGGATCACCAGCCTTT  
TGCAAATGCACACGATGTGCTAGCCCGCTCCCGCAGTCGAGCCAACGTGCTGAACAAGGTAG  
AATATGCACAGCAGCGCTGGAAGCTTCAAGTCCAAGAGCAGCGAAAGTCTGTCTTTGACCGG  
CATGTTGTCCTCAGC**TAA**TTGGGAATTGAATTCAAGGTGACTAGAAAGAAACAGGCAGACAA  
CTGGAAAGAACTGACTGGGTTTTGCTGGGTTTCATTTTAATACCTTGTTGATTTACCAACT  
GTTGCTGGAAGATTCAAACTGGAAGCAAAACTTGCTTGATTTTTTTTTCTTGTTAACGTA  
ATAATAGAGACATTTTTTAAAGCACACAGCTCAAAGTCAGCCAATAAGTCTTTTCCTATTTG  
TGACTTTTACTAATAAAAATAAATCTGCCTGTAAATTATCTTGAAGTCCTTTACCTGGAACA  
AGCACTCTCTTTTTTACCACATAGTTTTTAACCTTGACTTTCAAGATAATTTTCAGGGTTTTTG  
TTGTTGTTGTTTTTTGTTTGTTTGTTTGGTGGGAGAGGGGAGGGATGCCTGGGAAGTGGTT  
AACAACTTTTTTCAAGTCACTTTACTAAACAACTTTTGTAATAGACCTTACCTTCTATTT  
TCGAGTTTCATTTATATTTTGCAGTGTAGCCAGCCTCATCAAAGAGCTGACTTACTCATTTG  
ACTTTTGCCTGACTGTATTATCTGGGTATCTGCTGTGTCTGCACTTCATGGTAAACGGGAT  
CTAAAATGCCTGGTGGCTTTTCACAAAAGCAGATTTTCTTCATGTACTGTGATGTCTGATG  
CAATGCATCCTAGAACAACTGGCCATTTGCTAGTTTACTCTAAAGACTAAACATAGTCTTG  
GTGTGTGTGGTCTTACTCATCTTCTAGTACCTTTAAGGACAAATCCTAAGGACTTGGACACT  
TGCAATAAAGAAATTTTATTTTAAACCCAAGCCTCCCTGGATTGATAATATATACACATTTG  
TCAGCATTTCCGGTCGTGGTGAGAGGCAGCTGTTTGAGCTCCAATATGTGCAGCTTTGAACT  
AGGGCTGGGGTTGTGGGTGCCTCTTCTGAAAGGTCTAACCATTATTGGATAACTGGCTTTTT  
TCTTCCTATGTCCTCTTTGGAATGTAACAATAAAAATAATTTTTGAAACATCAA



300/330

**FIGURE 300**

MATLWGGLRLGSLLSLSCLALSVLLLAQLSDAAKNFEDVRCKCICPPYKENS  
GHYINKNIS  
QKDCDCLHVVEPMPVRGPDVEAYCLRCECKYEERSVTIKVTIIIIYLSILG  
LLLLLYMVYLT  
LVEPILKRRLFGHAQLIQSDDDIGDHQPFANAHDVLRSSRSRANVLNKVEYA  
QQRWKLQVQEQ  
RKSVFDRHVLS

301/330

**FIGURE 301**

GCACCTGCGACCACCGTGAGCAGTC**ATG**GCGTACTCCACAGTGCAGAGAGTCGCTCTGGCTT  
CTGGGGCTTGTCCTGGCTCTGTCGCTGCTGCTGCCCCAAGGCCTTCCTGTCCCGCGGGAAGCGG  
CAGGAGCCGCGCCGACACCTGAAGGAAAATTGGGCCGATTTCCACCTATGATGCATCATCA  
CCAGGCACCCTCAGATGGCCAGACTCCTGGGGCTCGTTTCCAGAGGTCTCACCTTGCCGAGG  
CATTTGCAAAGGCCAAAGGATCAGGTGGAGGTGCTGGAGGAGGAGGTAGTGGAAGAGGTCTG  
ATGGGGCAGATTATTCCAATCTACGGTTTTGGGATTTTTTTATATATACTGTACATTCTATT  
TAAGGTAAGTAGAATCATCCTAATCATATTACATCAAT**TGA**AAATCTAATATGGCGATAAAAA  
TCATTGTCTACATTAAAACTTCTTATAGTTCATAAAATTATTTCAAATCCATCATCTCTTTA  
AATCCTGCCTCCTCTTCATGAGGTACTTAGGATAGCCATTATTTTCAGTTTTCACATAAGAATG  
TTTACTCAATGTTTAAAGTGTTTTGCCCCAAAATTCACAACAAAGGCAGAACTAGGACTT  
GAACATGGATCTTTTGGTTCTTAATCCAGTGAGTGATACAATTCAATGCACTCCCCTGCCA

302/330

**FIGURE 302**

MAYSTVQRVALASGLVLALSLLLPKAFLSRGKRQEPPPTPEGKLGRFPMMHHHQAPSDGQT  
PGARFQRSHLAEAFKAKGSGGGAGGGGSGRGLMGQIIPIYGFIFLYILYILFKVSRIILI  
ILHQ

303/330

**FIGURE 303**

CGGCTCGAGTGCAGCTGTGGGGAGATTTTCAGTGCATTGCCTCCCCTGGGTGCTCTTCATCTT  
GGATTTGAAAGTTGAGAGCAGC**ATG**TTTTGCCCACTGAAACTCATCCTGCTGCCAGTGTTAC  
TGGATTATTCCTTGGGCCTGAATGACTTGAATGTTTCCCCGCCTGAGCTAACAGTCCATGTG  
GGTGATTTCAGCTCTGATGGGATGTGTTTTCCAGAGCACAGAAGACAAATGTATATTCAAGAT  
AGACTGGACTCTGTCCACCAGGAGAGCACGCCAAGGACGAATATGTGCTATACTATTACTCCA  
ATCTCAGTGTGCCTATTGGGCGCTTCCAGAACCGCGTACACTTGATGGGGGACATCTTATGC  
AATGATGGCTCTCTCCTGCTCCAAGATGTGCAAGAGGCTGACCAGGGAACCTATATCTGTGA  
AATCCGCCTCAAAGGGGAGAGCCAGGTGTTCAAGAAGGCGGTGGTACTGCATGTGCTTCCAG  
AGGAGCCCCAAAGAGCTCATGGTCCATGTGGGTGGATTGATTTCAGATGGGATGTGTTTTCCAG  
AGCACAGAAGTGAAACACGTGACCAAGGTAGAATGGATATTTTCAGGACGGCGCGCAAAGGA  
GGAGATTGTATTTTCGTTACTACCACAACTCAGGATGTCTGTGGAGTACTCCCAGAGCTGGG  
GCCACTTCCAGAATCGTGTGAACCTGGTGGGGGACATTTTCCGCAATGACGGTTCCATCATG  
CTTCAAGGAGTGAGGGAGTCAGATGGAGGAACTACACCTGCAGTATCCACCTAGGGAACCT  
GGTGTTCAGAAAACCATTTGTGCTGCATGTCAGCCCGGAAGAGCCTCGAACACTGGTGACCC  
CGGCAGCCCTGAGGCCTCTGGTCTTGGGTGGTAATCAGTTGGTGATCATTGTGGGAATTGTCT  
TGTGCCACAATCCTGCTGCTCCCTGTTCTGATATTGATCGTGAAGAAGACCTGTGGAAATAA  
GAGTTCAGTGAATTCTACAGTCTTGGTGAAGAACACGAAGAAGACTAATCCAGAGATAAAAG  
AAAAACCCTGCCATTTTGAAAGATGTGAAGGGGAGAAACACATTTACTCCCCAATAATTGTA  
CGGGAGGTGATCGAGGAAGAAGAACCAAGTGAAAAATCAGAGGCCACCTACATGACCATGCA  
CCCAGTTTGGCCTTCTCTGAGGTCAGATCGGAACAACCTCACTTGAAAAAAGTCAGGTGGGG  
GAATGCCAAAAACACAGCAAGCCTTT**TGA**GAGAAGATGGAGAGTCCCTTCATCTCAGCAGCGG  
TGGAGACTCTCTCCTGTGTGTGTCCTGGGCCACTCTACCAGTGATTTTCAGACTCCCGCTCTC  
CCAGCTGTCCTCCTGTCTCATTGTTTGGTCAATACACTGAAGATGGAGAATTTGGAGCCTGG  
CAGAGAGACTGGACAGCTCTGGAGGAACAGGCCTGCTGAGGGGAGGGGAGCATGGACTTGGC  
CTCTGGAGTGGGACACTGGCCCTGGGAACCAGGCTGAGCTGAGTGGCCTCAAACCCCCCGTT  
GGATCAGACCCTCCTGTGGGCAGGGTTCTTAGTGGATGAGTTACTGGGAAGAATCAGAGATA  
AAAACCAACCCAAATCAA

304/330

**FIGURE 304**

MFCPLKLILLPVLLDYSLGLNDLNVSPPELTVHVGDSALMGCVFQSTEDKCIFKIDWTLSPG  
EHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDILCNDGSLLLQDVQEADQGTYICEIRLKGES  
QVFKKAVVLHVLPEEPKELMVHVGGLIQMGCVFQSTEVKHVTKVEWIFSGRRAKEEIVFRYY  
HKLRMSVEYSQSWGHFQNRVNLVGDI FRNDGSIMLQGVRES DGGNYTCSIHLGNLVFKKTIV  
LHVSPEEPRTLVT PAALRPLVLGGNQLVIIVGIVCATILLLPVLILIVKKT CGNKSSVNSTV  
LVKN TKTNPEIKEKPCHFERCEGEKHIYSPIIVREVIEEEEPSEKSEATYMTMHPVWPSLR  
SDRNNSLEKKSGGGMPKTQQAF

305/330

**FIGURE 305**

CTATGAAGAAGCTTCCTGGAAAACAATAAGCAAAGGAAAACAAATGTGTCCCATCTCACATG  
GTTCTACCCTACTAAAGACAGGAAGATCATAAACTGACAGATACTGAAATTGTAAGAGTTGG  
AAACTACATTTTGCAAAGTCATTGAACTCTGAGCTCAGTTGCAGTACTCGGGAAGCC**ATG**CA  
GGATGAAGATGGATACATCACCTTAAATATTAAAACCTCGGAAACCAGCTCTCGTCTCCGTTG  
GCCCTGCATCCTCCTCCTGGTGGCGTGTGATGGCTTTGATTCTGCTGATCCTGTGCGTGCGG  
ATGGTTGTCTGGGCTGGTGGCTCTGGGGATTTGGTCTGTCATGCAGCGCAATTACCTACAAGA  
TGAGAATGAAAATCGCACAGGAACCTGCAACAATTAGCAAAGCGCTTCTGTCAATATGTGG  
TAAAACAATCAGAACTAAAGGGCACTTTCAAAGGTCATAAATGCAGCCCCTGTGACACAAAC  
TGGAGATATTATGGAGATAGCTGCTATGGGTTCTTCAGGCACAACCTAACATGGGAAGAGAG  
TAAGCAGTACTGCACTGACATGAATGCTACTCTCCTGAAGATTGACAACCGGAACATTGTGG  
AGTACATCAAAGCCAGGACTCATTTAATTCGTTGGGTCGGATTATCTCGCCAGAAGTCGAAT  
GAGGTCTGGAAGTGGGAGGATGGCTCGGTTATCTCAGAAAATATGTTTGAGTTTTTGGAAGA  
TGGAAAAGGAAATATGAATTGTGCTTATTTTCATAATGGGAAAATGCACCCTACCTTCTGTG  
AGAACAAACATTATTTAATGTGTGAGAGGAAGGCTGGCATGACCAAGGTGGACCAACTACCT  
**TAA**TGCAAAGAGGTGGACAGGATAACACAGATAAGGGCTTTATTGTACAATAAAAGATATGT  
ATGAATGCATCAGTAGCTGAAAAAAAAAAAAA

306/330

**FIGURE 306**

MQDEDGYITLNIKTRKPALVSVGPASSSWWRVMALILLILCVGMVVGLVALGIWSVMQRNYL  
QDENENRTGTLQQLAKRFCQYVVKQSELKGTFKGHKCSPCDTNWRYYGDSYGFRRHNLWE  
ESKQYCTDMNATLLKIDNRNIVEYIKARTHLIRWVGLSRQKSNEVWKWEDGSVISENMFEEFL  
EDGKGNMNCAYFHNGKMHPTFCENKHYLMCERKAGMTKVDQLP

307/330

**FIGURE 307**

CCCACGCGTCCGCGCAGTCGCGCAGTTCTGCCTCCGCCTGCCAGTCTCGCCCGCGATCCCGG  
CCCGGGGCTGTGGCGTCGACTCCGACCCAGGCAGCCAGCAGCCCCGCGCGGGAGCCGGACCGC  
CGCCGGAGGAGCTCGGACGGCATGCTGAGCCCCCTCCTTTGCTGAAGCCCGAGTGCGGAGAA  
GCCCCGGGCAAACGCAGGCTAAGGAGACCAAAGCGGCGAAGTCGCGAGACAGCGGACAAGCAG  
CGGAGGAGAAGGAGGAGGAGGCGAACCCAGAGAGGGGCAGCAAAAGAAGCGGTGGTGGTGGG  
CGTCGTGGCC**ATG**GCGGCGGCTATCGCCAGCTCGCTCATCCGTCAGAAGAGGCAAGCCCGCG  
AGCGCGAGAAATCCAACGCCTGCAAGTGTGTCAGCAGCCCCAGCAAAGGCAAGACCAGCTGC  
GACAAAAACAAGTTAAATGTCTTTTCCCGGGTCAAACCTCTTCGGCTCCAAGAAGAGGCGCAG  
AAGAAGACCAGAGCCTCAGCTTAAGGGTATAGTTACCAAGCTATACAGCCGACAAGGCTACC  
ACTTGCAGCTGCAGGCGGATGGAACCATTGATGGCACCAAAGATGAGGACAGCACTTACACT  
CTGTTTAACCTCATCCCTGTGGGTCTGCGAGTGGTGGCTATCCAAGGAGTTCAAACCAAGCT  
GTACTTGGCAATGAACAGTGAGGGATACTTGTACACCTCGGAACTTTTACACCTGAGTGCA  
AATTCAAAGAATCAGTGTTTGAAAATTATTATGTGACATATTCATCAATGATATACCGTCAG  
CAGCAGTCAGGCCGAGGGTGGTATCTGGGTCTGAACAAAGAAGGAGAGATCATGAAAGGCAA  
CCATGTGAAGAAGAACAAGCCTGCAGCTCATTTTCTGCCTAAACCACTGAAAGTGGCCATGT  
ACAAGGAGCCATCACTGCACGATCTCACGGAGTTCTCCCGATCTGGAAGCGGGACCCCAACC  
AAGAGCAGAAGTGTCTCTGGCGTGCTGAACGGAGGCAAATCCATGAGCCACAATGAATCAAC  
G**TAG**CCAGTGAGGGCAAAAGAAGGGCTCTGTAACAGAACCTTACCTCCAGGTGCTGTTGAAT  
TCTTCTAGCAGTCCTTCACCCAAAAGTTCAAATTTGTCAGTGACATTTACCAAACAAACAGG  
CAGAGTTCATATTCTATCTGCCATTAGACCTTCTTATCATCCATACTAAAGC



308/330

**FIGURE 308**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA28498

&gt;&lt;subunit 1 of 1, 245 aa, 1 stop

&gt;&lt;MW: 27564, pI: 10.18, NX(S/T): 1

MAAAIASSLIRQKRQAREREKSNACKCVSSPSKGKTSCDKNKLNVFSRVKLFSGSKRRRRRP  
EPQLKGIVTKLYSRQGYHLQLQADGTIDGTKDEDSTYTLFNLI PVGLRVVAIQGVQTKLYLA  
MNSEGILYTSELFTPECKFKESVFENYYVTYSSMIYRQQQSGRGWYLGLNKEGEIMKGNHVK  
KNKPAAHFLPKPLKVAMYKEPSLHDLTEFSRSGSGTPTKRSVSGLNGGKSMHNEST

**N-glycosylation site.**

amino acids 242-246

**Glycosaminoglycan attachment site.**

amino acids 165-169, 218-222

**Tyrosine kinase phosphorylation site.**

amino acids 93-100

**N-myristoylation site.**

amino acids 87-93, 231-237

**ATP/GTP-binding site motif A (P-loop).**

amino acids 231-239

**HBGF/FGF family proteins**

amino acids 78-94, 102-153

309/330

**FIGURE 309**

CCAGGATGGAGCTGGGGCCTGTATAGCCATATTATTGTTCTATGCTACTAGACATGGGGGGG  
ACTTGGTGAAAAAGGTATTATCCAGCCAGAGGGTCTGGGAGCCCTGTCTTACTGAACCTGGG  
CAACCTGGATATTCTGAGACATATTTTGGGGGGATTTTCAGTGAAAAAGTGGGGGATCCCCT  
CCATTTAGAGTGTAGCAAAGGAAAAAACACCAAGGTTGGGTCCTTCCTGACATTGGCAGTG  
CCCCAGTAGGGGTGGGATGAGCGAATATTCCCAAAGCTAAAGTCCACACCCCTGTAGATTAC  
AAGAGTGGATTTGGCAGGAGTGTGCCCCAAAATACAGTGGAAGGTGCCTGAAGATATTTAA  
ACCACGTCTTGGAATTTAGTGGGTCTTGGCTTTGGGATAGGTGAAGTGAGGACAGACACTG  
GAGAGGAGGGAAAGGGGACGTTTTCAATAGGAGGCAAACTCGAGGGTGGGATCCACTGAGG  
AGTACATAGGCTGCTGGATCTGGTGGAGCCAGCACTGGGCCCACGGGTGGTAACCTGGCTGCT  
GTGGAGGGGGGTACGTGAGGGGGGGGTCTGGGGCTTATCCTCAGGTCCTGTGGGTGGGGCAG  
CGAGTCGGGGCCTGAGCGTCAAGAGCATGCCCTAGTGAGCGGGCTCCTCTGGGGGAGCCCAG  
CGCGCTCCGGGCGCCTGCCGGTTTGGGGGTGTCTCCTCCCGGGGCGCT**ATG**GCGGCGCTGGC  
CAGTAGCCTGATCCGGCAGAAGCGGGAGGTCCGCGAGCCCGGGGGCAGCCGGCCGGTGTGCG  
CGCAGCGGCGCGTGTGTCCCCGCGGCACCAAGTCCCTTTGCCAGAAGCAGCTCCTCATCCTG  
CTGTCCAAGGTGCGACTGTGCGGGGGGCGGCCCCGCGCGGCCGGACCGCGGCCCGGAGCCTCA  
GCTCAAAGGCATCGTCACCAAACCTGTTCTGCCGCCAGGGTTTCTACCTCCAGGCGAATCCCG  
ACGGAAGCATCCAGGGCACCCAGAGGATACCAGCTCCTTCACCCACTTCAACCTGATCCCT  
GTGGGCCTCCGTGTGGTCACCATCCAGAGCGCCAAGCTGGGTCACTACATGGCCATGAATGC  
TGAGGGACTGCTCTACAGTTCGCCGCATTTACAGCTGAGTGTGCTTTAAGGAGTGTGTCT  
TTGAGAATTACTACGTCCTGTACGCCTCTGCTCTCTACCGCCAGCGTCGTTCTGGCCGGGCC  
TGGTACCTCGGCCTGGACAAGGAGGGCCAGGTCATGAAGGGAAACCGAGTTAAGAAGACCAA  
GGCAGCTGCCCACTTTCTGCCCAAGCTCCTGGAGGTGGCCATGTACCAGGAGCCTTCTCTCC  
ACAGTGTCCCCGAGGCCTCCCCTTCCAGTCCCCCTGCCCCC**TGA**AATGTAGTCCCTGGACTG  
GAGGTTCCCTGCACTCCCAGTGAGCCAGCCACCACCACAACCTGT

310/330

## **FIGURE 310**

MAALASSLIRQKREVPGGSRPVSAQRRVCPRGTKSLCQKQLLILLSKVRLCGGRPARPDR  
GPEPQLKGIIVTKLFCRQGFIYLQANPDGSIQGTPEDTSSFTHFNLIPVGLRVVTIQSAKLGHY  
MAMNAEGLLYSSPHFTAECRFKECVFENYYVLYASALYRQRRSGRAWYLGLDKEGQVMKGNR  
VKKTKAAAHFLPKLLEVAMYQEPSLHSVPEASPSPPAP

**Tyrosine kinase phosphorylation site:**

amino acids 199-207

**N-myristoylation sites:**

amino acids 54-60, 89-95, 131-137

**HBGF/FGF family signature:**

amino acids 131-155

311/330

**FIGURE 311**

**ATG**GCCGCGGCCATCGCTAGCGGCTTGATCCGCCAGAAGCGGCAGGCGCGGGAGCAGCACTG  
GGACCGGCCGTCTGCCAGCAGGAGGCGGAGCAGCCCCAGCAAGAACCGCGGGCTCTGCAACG  
GCAACCTGGTGGATATCTTCTCCAAAGTGCGCATCTTCGGCCTCAAGAAGCGCAGGTTGCGG  
CGCCAAGATCCCCAGCTCAAGGGTATAGTGACCAGGTTATATTGCAGGCAAGGCTACTACTT  
GCAAATGCACCCCGATGGAGCTCTCGATGGAACCAAGGATGACAGCACTAATTCTACACTCT  
TCAACCTCATAACCAGTGGGACTACGTGTTGTTGCCATCCAGGGAGTGAAAACAGGGTTGTAT  
ATAGCCATGAATGGAGAAGGTTACCTCTACCCATCAGAACTTTTTACCCCTGAATGCAAGTT  
TAAAGAATCTGTTTTTGAAAATTATTATGTAATCTACTCATCCATGTTGTACAGACAACAGG  
AATCTGGTAGAGCCTGGTTTTTTGGGATTAAATAAGGAAGGGCAAGCTATGAAAGGGAACAGA  
GTAAAGAAAACCAAACCAGCAGCTCATTTTCTACCCAAGCCATTGGAAGTTGCCATGTACCG  
AGAACCATCTTTGCATGATGTTGGGGAAACGGTCCCGAAGCCTGGGGTGACGCCAAGTAAAA  
GCACAAGTGCGTCTGCAATAATGAATGGAGGCAAACCAGTCAACAAGAGTAAGACAACA**TAG**

312/330

**FIGURE 312**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA28503

&gt;&lt;subunit 1 of 1, 247 aa; 1 stop

&gt;&lt;MW: 27702, pI: 10.36, NX(S/T): 2

MAAAIASGLIRQKRQAREQHWDRPSASRRRSSPSKNRGLCNGNLVDIFSKVRI FGLKKRRLR  
RQDPQLKGIVTRL YCRQGYLQMHDPD GALTGDKDDSTNSTLFNLIPVGLRVVAIQGVKTGLY  
IAMNGEGYLYPSELF TPECKFKESVFENYYVIYSSMLYRQQESGRAWFLGLNKEGQAMKGNR  
VKKTKPAAHFLPKPLEVAMYREPSLHDVGETVPKPGVTPSKSTSASAIMNGGKPVNKS KTT

**N-glycosylation site.**

amino acids 100-104, 242-246

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 28-32, 29-33

**Tyrosine kinase phosphorylation site.**

amino acids 199-207

**N-myristoylation site.**

amino acids 38-44, 89-95, 118-124, 122-128, 222-228

**HBGF/FGF family proteins.**

amino acids 104-155, 171-198

313/330

**FIGURE 313**

GGGGAGAGGAATTGACCATGTAAAAGGAGACTTTTTTTTTTGGTGGTGGTGGCTGTTGGGTGCCTTGCAAAAAT  
GAAGGATGCAGGACGCAGCTTTCTCCTGGAACCGAACGCAATGGATAAACTGATTGTGCAAGAGAGAAGGAAGA  
ACGAAGCTTTTTCTTGTGAGCCCTGGATCTTAACACAAATGTGTATATGTGCACACAGGGAGCATTCAAGAATG  
AAATAAACAGAGTTAGACCCGCGGGGGTGGTGTGTTCTGACATAAATAAATAATCTTAAAGCAGCTGTTCCC  
CTCCCCACCCCCAAAAAAGGATGATTGGAATGAAGAACCGAGGATTCACAAAGAAAAAGTATGTTCAATTT  
TTCTCTATAAAGGAGAAAGTGAGCCAAGGAGATATTTTTGGAATGAAAAGTTTGGGGCTTTTTTAGTAAAGTAA  
AGAAGTGGTGTGGTGGTGTTCCTTTCTTTTGAATTTCCACAAAGAGGAGAGGAAATTAATAATACATCTGC  
AAAGAAATTTTCAAGAGAAGAAAGTTGACCGCGGCAGATTGAGGCATTGATTGGGGGAGAGAAACCAGCAGAGCA  
CAGTTGGATTTGTGCCTATGTTGACTAAAAATTGACGGATAATTGCAGTTGGATTTTTCTTCATCAACCTCCTTT  
TTTTTAAATTTTTATTCTTTTGGTATCAAGATCATGCGTTTTCTCTTGTCTTAACCACCTGGATTTCCATCT  
GGATGTTGCTGTGATCAGTCTGAAATACAACCTGTTTGAATTCAGAAGGACCAACACCAGATAAATTATGAATG  
TTGAACAAGATGACCTTACATCCACAGCAGATAATGATAGGTCTAGGTTTAACAGGGCCCTATTTGACCCCT  
GCTTGTGGTGTGCTGGCTCTTCAACTTCTTGTGGTGGCTGGTCTGGTGC GGCTCAGACCTGCCCTTCTGTGT  
GCTCCTGCAGCAACCAGTTCAGCAAGGTGATTTGTGTTTCGGA AAAACCTGCGTGAGGTTCCGGATGGCATCTCC  
ACCAACACACGGCTGCTGAACCTCCATGAGAACCAAATCCAGATCATCAAAGTGAACAGCTTCAAGCACTTGAG  
GCACTTGGAATCCTACAGTTGAGTAGGAACCATATCAGAACCATTGAAATTGGGGCTTTCAATGGTCTGGCGA  
ACCTCAACACTCTGGAACCTCTTGACAATCGTCTTACTACCATCCCGAATGGAGCTTTTGTATACTTGTCTAAA  
CTGAAGGAGCTCTGGTTGCGAAACAACCCCATTGAAAGCATCCCTTCTTATGCTTTTAACAGAATTCCTTCTTT  
GCGCCGACTAGACTTAGGGGAATTGAAAAGACTTTCATACATCTCAGAAGGTGCCTTTGAAGGTCTGTCCAAC  
TGAGGTATTTGAACCTTGCCATGTGCAACCTTCGGGAAATCCCTAACCTCACACCGCTCATAAACTAGATGAG  
CTGGATCTTTCTGGGAATCATTTATCTGCCATCAGGCCTGGCTCTTTCCAGGGTTTGATGCACCTTCAAAAAC  
GTGGATGATACAGTCCCAGATTCAAGTGATTGAACGGAATGCCTTTGACAACCTTCAGTCACTAGTGGAGATCA  
ACCTGGCACACAATAATCTAACATTACTGCCTCATGACCTCTTCACTCCCTTGATCATCTAGAGCGGATACAT  
TTACATCACAACCTTGGAACCTGTAACCTGTGACATACTGTGGCTCAGCTGGTGGATAAAAAGACATGGCCCCCTC  
GAACACAGCTTGTTGTGCCCCGGTGTAACACTCCTCCCAATCTAAAGGGGAGGTACATTGGAGAGCTCGACCAGA  
ATTACTTCACATGCTATGCTCCGGTGATTGTGGAGCCCCCTGCAGACCTCAATGTCACTGAAGGCATGGCAGCT  
GAGCTGAAATGTCGGGCCTCCACATCCCTGACATCTGTATCTTGGATTACTCCAAATGGAACAGTCATGACACA  
TGGGGCGTACAAAGTGCGGATAGCTGTGCTCAGTGATGGTACGTTAAATTTACAAATGTAACCTGTGCAAGATA  
CAGGCATGTACACATGTATGGTGAGTAATTCCGTTGGGAATACTACTGCTTCAGCCACCTGAATGTTACTGCA  
GCAACCACTACTCCTTTCTCTTACTTTTCAACCGTCACAGTAGAGACTATGGAACCGTCTCAGGATGAGGCACG  
GACCACAGATAACAATGTGGGTCCCACTCCAGTGCTGACTGGGAGACCACCAATGTGACCACCTCTCTCACAC  
CACAGAGCACAAGGTCGACAGAGAAAACCTTCACCATCCAGTGACTGATATAAACAGTGGGATCCCAGGAATT  
GATGAGGTCATGAAGACTACCAAAATCATCATTGGGTGTTTTGTGGCCATCACACTCATGGCTGCAGTGATGCT  
GGTCATTTTCTACAAGATGAGGAAGCAGCACCATCGGCAAAACCATCACGCCCCAACAAAGGACTGTTGAAATTA  
TTAATGTGGATGATGAGATTACGGGAGACACACCCATGGAAAGCCACCTGCCATGCCTGCTATCGAGCATGAG  
CACCTAAATCACTATAACTCATACAAATCTCCCTTCAACCACACAACAACAGTTAACACAATAAATTCATACA  
CAGTTCAGTGCATGAACCGTTATTGATCCGAATGAACTCTAAAGACAATGTACAAGAGACTCAAATCTAAACA  
TTTACAGAGTTACAAAAACAACAATCAAAAAAAGACAGTTTATTAAAAATGACACAAATGACTGGGCTAA  
ATCTACTGTTTCAAAAAAGTGCTTTACAAAAAACA AAAAGAAATTTATTTATTA AAAATTCATTG  
TGATCTAAAGCAGACAAAA

314/330

**FIGURE 314**

MLNKMTLHPQQIMIGPRFNRALFDPLLVLALLQLLVVAGLVRAQTCPSVCSCSNQFSKVIC  
VRKNLREVPDGI STNTRLLNLHENQIQIIKVNSFKHLRHLEILQLSRNHIRTIEIGAFNGLA  
NLNTLELFDNRLTTIPNGAFVYLSKLKELWLRNNPIESIPSYAFNRIPSLRRLDLGELKRLS  
YISEGAFEGLSNRLRYLNLAMCNLREIPNLTPLIKLELDL SGNHLSAIRPGSFQGLMHLQKL  
WMIQSQIQVIERNAFDNLQSLVEINLAHNNLTLLPHDLFTPLHHLERIHLLHNPWNCNCDIL  
WLSWWIKDMAPSNTACCARCNTPPNLKGRYIGELDQNYFTCYAPVIVEPPADLNVTEGMAAE  
LKCRASTSLTSVSWITPNGTVMTHGAYKVRIAVLS DGT LNFTNVT VQDTGMYTCMVSN SVGN  
TTASATLNVTAATTT PFSYFSTVTVETMEPSQDEARTTDNNVGPTPVVDWETTNVTTSLTPQ  
STRSTKFTFTIPVTDINS GIPGIDEVMKTTKIIIGCFVAITLMAAVMLVIFYKMRKQHRQN  
HHAPTRTVEIINVDDEITGDTPMESHLPMPAIEHEHLNHYSYKSPFNHTTTVNTINSIHSS  
VHEPLLIRMNSKDNVQETQI

**Signal sequence:**

amino acids 1-44

**Transmembrane domain:**

amino acids 523-543

**N-glycosylation site.**amino acids 278-282, 364-368, 390-394, 412-416, 415-419,  
434-438, 442-446, 488-492, 606-610**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 183-187

**Casein kinase II phosphorylation site.**

amino acids 268-272, 417-421, 465-469, 579-583, 620-624

**N-myristoylation site.**amino acids 40-46, 73-79, 118-124, 191-197, 228-234, 237-243,  
391-397, 422-428, 433-439, 531-537

315/330

**FIGURE 315**

GCGCCGGGAGCCCATCTGCCCCCAGGGGCGCGGGGCGGGCTCCCGCCCCGGCACAT  
GGCTGCAGCCACCTCGCGCGCACCCCGAGGCGCCGCGCCAGCTCGCCCGAGGTCCGTGGA  
GGCGCCCCGGCCGCCCCGGAGCCAAGCAGCAACTGAGCGGGGAAGCGCCCGCGTCCGGGGATC  
GGG**ATG**TCCCTCCTCCTTCTCCTCTTGCTAGTTTTCTACTATGTTGGAACCTTGGGGACTCA  
CACTGAGATCAAGAGAGTGGCAGAGGAAAAGGTCACCTTGCCCTGCCACCATCAACTGGGGC  
TTCCAGAAAAAGACACTCTGGATATTGAATGGCTGCTCACCGATAATGAAGGGAACCAAAAA  
GTGGTGATCACTTACTCCAGTCGTCATGTCTACAATAACTTGACTGAGGAACAGAAGGGCCG  
AGTGGCCTTTGCTTCCAATTTCTGGCAGGAGATGCCTCCTTGAGATTGAACCTCTGAAGC  
CCAGTGATGAGGGCCGGTACACCTGTAAGGTAAAGAATTCAGGGCGCTACGTGTGGAGCCAT  
GTCATCTTAAAAGTCTTAGTGAGACCATCCAAGCCCAAGTGTGAGTTGGAAGGAGAGCTGAC  
AGAAGGAAGTGACCTGACTTTGCAGTGTGAGTCATCCTCTGGCACAGAGCCCATTGTGTATT  
ACTGGCAGCGAATCCGAGAGAAAGAGGGAGAGGATGAACGTCTGCCTCCCAAATCTAGGATT  
GACTACAACCACCCTGGACGAGTTCTGCTGCAGAATCTTACCATGTCCTACTCTGGACTGTA  
CCAGTGACACAGCAGGCAACGAAGCTGGGAAGGAAAGCTGTGTGGTGCGAGTAAGTGTACAGT  
ATGTACAAAGCATCGGCATGGTTGCAGGAGCAGTGACAGGCATAGTGGCTGGAGCCCTGCTG  
ATTTTCCTCTTGTTGGTGTGGCTGCTAATCCGAAGGAAAGACAAAGAAAGATATGAGGAAGAAGA  
GAGACCTAATGAAATTCGAGAAGATGCTGAAGCTCCAAAAGCCCGTCTTGTAACCCAGCT  
CCTCTTCCTCAGGCTCTCGGAGCTCACGCTCTGGTTCTTCCTCCACTCGCTCCACAGCAAAT  
AGTGCCTCACGCAGCCAGCGGACACTGTCAACTGACGCAGCACCCAGCCAGGGCTGGCCAC  
CCAGGCATACAGCCTAGTGGGGCCAGAGGTGAGAGGTTCTGAACCAAAGAAAGTCCACCATG  
CTAATCTGACCAAAGCAGAAACCACACCCAGCATGATCCCCAGCCAGAGCAGAGCCTTCCAA  
ACGGTCT**TGA**ATTACAATGGACTTGACTCCCACGCTTTCTAGGAGTCAGGGTCTTTGGACTC  
TTCTCGTCATTGGAGCTCAAGTCACCAGCCACACAACCAGATGAGAGGTCATCTAAGTAGCA  
GTGAGCATTGCACGGAACAGATTCAGATGAGCATTTTCCTTATAACAATACCAAACAAGCAAA  
AGGATGTAAGCTGATTCATCTGTAAAAAGGCATCTTATTGTGCCTTTAGACCAGAGTAAGGG  
AAAGCAGGAGTCCAAATCTATTTGTTGACCAGGACCTGTGGTGAGAAGGTTGGGGAAAGGTG  
AGGTGAATATACCTAAACTTTTAATGTGGGATATTTTGTATCAGTGCTTTGATTCACAATT  
TTCAAGAGGAAATGGGATGCTGTTTGTAATTTTCTATGCATTTCTGCAAACCTTATTGGATT  
ATTAGTTATTGAGACAGTCAAGCAGAACCCACAGCCTTATTACACCTGTCTACACCATGTAC  
TGAGCTAACCCTTCTAAGAACTCCAAAAAAGGAAACATGTGTCTTCTATTCTGACTTAAC  
TTCATTTGTCATAAGGTTTGGATATTAATTTCAAGGGGAGTTGAAATAGTGGGAGATGGAGA  
AGAGTGAATGAGTTTCTCCCACTCTATACTAATCTCACTATTTGTATTGAGCCCAAAATAAC  
TATGAAAGGAGACAAAAATTTGTGACAAAGGATTGTGAAGAGCTTCCATCTTCATGATGTT  
ATGAGGATTGTTGACAAACATTAGAAATATATAATGGAGCAATTGTGGATTTCCTCAAAT  
CAGATGCCTCTAAGGACTTTCCTGCTAGATATTTCTGGAAGGAGAAAATACAACATGTCATT  
TATCAACGTCCTTAGAAAGAATTCTTCTAGAGAAAAAGGGATCTAGGAATGCTGAAAGATTA  
CCCAACATAACATTATAGTCTCTTCTTCTGAGAAAATGTGAAACCAGAATTGCAAGACTGG  
GTGGACTAGAAAGGGAGATTAGATCAGTTTTCTCTTAATATGTCAAGGAAGGTAGCCGGGCA  
TGGTGCCAGGCACCTGTAGGAAAATCCAGCAGGTGGAGGTTGCAGTGAGCCGAGATTATGCC  
ATTGCACTCCAGCCTGGGTGACAGAGCGGGACTCCGTCTC



316/330

**FIGURE 316**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA45419

&gt;&lt;subunit 1 of 1, 373 aa, 1 stop

&gt;&lt;MW: 41281, pI: 8.33, NX(S/T): 3

MSLLLLLLLLVSYYVGTGLGTHTEIKRVAEEKVTLPCHHQLGLPEKDTLDIEWLLTDNEGNQKV  
VITYSSRHVYNNLTTEEQKGRVAFASNFLAGDASLQIEPLKPSDEGRYTCKVKNSGRYVWSHV  
ILKVLVRPSKPKCELEGELTEGSDTLQCESSSGTEPIVYYWQRIREKEGEDERLPPKSRID  
YNHPGRVLLQNLTMSYSGLYQCTAGNEAGKESCVVRVTVQYVQSIGMVAGAVTGIVAGALLI  
FLLVWLLIRRKDKERYEEEEERPNEIREDAEAPKARLVKPSSSSSGSRSSRSGSSSTRSTANS  
ASRSQRTLSTDAAPQPGLATQAYSLVGPEVRGSEPKKVHHANLTKAETTPSMIPSQSRAFQTV

**Signal sequence:**

amino acids 1-16

**Transmembrane domain:**

amino acids 232-251

317/330

**FIGURE 317**

CGCGAGGCGCGGGGAGCCTGGGACCAGGAGCGAGAGCCGCCTACCTGCAGCCGCCGCCACGGCACGGCAGCCA  
CC**ATG**GCGCTCCTGCTGTGCTTCGTGCTCCTGTGCGGAGTAGTGGATTTGCCAGAAAGTTTGTAGTATCACTACT  
CCTGAAGAGATGATTGAAAAAGCCAAAGGGGAAACTGCCTATCTGCCATGCAAAATTACGCTTAGTCCCGAAGA  
CCAGGGACCGCTGGACATCGAGTGGCTGATATCACCAGCTGATAATCAGAAGGTGGATCAAGTGATTATTTTAT  
ATTCTGGAGACAAAATTTATGATGACTACTATCCAGATCTGAAAGGCCGAGTACATTTTACGAGTAATGATCTC  
AAATCTGGTGATGCATCAATAAATGTAACGAATTTACAACGTGTCAGATATTGGCACATATCAGTGCAAGTGAA  
AAAAGCTCCTGGTGTTGCAAATAAGAAGATTCATCTGGTAGTTCTTGTTAAGCCTTCAGGTGCGAGATGTTACG  
TTGATGGATCTGAAGAAATTGGAAGTGACTTTAAGATAAAATGTGAACCAAAAGAGGTTCACTTCCATTACAG  
TATGAGTGGCAAAAATTGTCTGACTCACAGAAAATGCCCACTTCATGGTTAGCAGAAAATGACTTCATCTGTTAT  
ATCTGTAAAAAATGCCTCTTCTGAGTACTCTGGGACATACAGCTGTACAGTCAGAAACAGAGTGGGCTCTGATC  
AGTGCCCTGTTGCGTCTAAACGTTGTCCCTCCTTCAAATAAAGCTGGACTAATTGCAGGAGCCATTATAGGAACT  
TTGCTTGCTCTAGCGCTCATTGGTCTTATCATCTTTTGCTGTGCTGTAAGGCGCAGAGAAGAAAAATATGAAAA  
GGAAGTTCATCACGATATCAGGGAAGATGTGCCACCTCCAAAGAGCCGTACGTCCACTGCCAGAAGCTACATCG  
GCAGTAATCATTCATCCCTGGGGTCCATGTCTCCTTCCAACATGGAAGGATATTCCAAGACTCAGTATAACCAA  
GTACCAAGTGAAGACTTTGAACGCACTCCTCAGAGTCCGACTCTCCCACTGCTAAGTTCAGTACCCTTACAA  
GACTGATGGAATTACAGTTGTAT**TAA**ATATGGACTACTGAAGAATCTGAAGTATTGTATTATTTGACTTTATTTT  
AGGCCCTCTAGTAAAGACTTAAATGTTTTTTAAAAAAAAGCACAAAGGCACAGAGATTAGAGCAGCTGTAAGAACAC  
ATCTACTTTTATGCAATGGCATTAGACATGTAAGTCAGATGTCATGTCAAATTAGTACGAGCCAAATTTCTTTGT  
TAAAAAACCCCTATGTATAGTGACACTGATAGTTAAAAGATGTTTTATTATATTTTCAATAACTACCACTAACAA  
ATTTTAACTTTTTCATATGCATATTCTGATATGTGGTCTTTTAGGAAAAGTATGGTTAATAGTTGATTTTTCAA  
AGGAAATTTTAAATTTCTTACGTTCTGTTTAATGTTTTTGCTATTTAGTTAAATACATTGAAGGGAATACCCG  
TTCTTTTCCCCTTTTATGCACACAACAGAAACACGCGTTGTATGCCTCAAACATTTTTTTATTTGCAACTACA  
TGATTTACACAATTTCTTTAAACAACGACATAAAATAGATTTCTCTTGATATATAAAATAACTTACATACGCTCCA  
TAAAGTAAATTTCTCAAAGGTGCTAGAACAAATCGTCCACTTCTACAGTGTTCTCGTATCCAACAGAGTTGATGC  
ACAAATATATAAATACTCAAGTCCAATATTAATAAATCTTAGGCCTTGACTAACTTTAATAAAATTTCTCAAACCTA  
TATCAATATCTAAAGTGCAATATTTTTTAAAGAAAGATTATTCTCAATAAATTTCTATAAAAAATAAGTTTGATGG  
TTTGGCCCATCTAACTTCACTACTATTAGTAAGAACTTTTAACTTTTAAATGTGTAGTAAGGTTTATTCTACCTT  
TTTCTCAACATGACACCAACACAATCAAAAACGAAGTTAGTGAGGTGCTAACATGTGAGGATTAATCCAGTGAT  
TCCGCTCACAAATGCATTCCAGGAGGAGGTACCCATGTCACTGGAATTGGGCGATATGGTTTATTTTTTCTTCCC  
TGATTTGGATAACCAATGGAACAGGAGGAGGATAGTGATTCTGATGGCCATTCCCTCGATACATTCCCTGGCTT  
TTTTCTGGGCAAAGGGTGCCACATTGGAAGAGGTGGAATATAAGTTCTGAAATCTGTAGGGAAGAGAACACAT  
TAAGTTAATTCAAAGGAAAAAATCATCATCTATGTTCCAGATTTCTCATTAAAGACAAAGTTACCCACAACACT  
GAGATCACATCTAAGTGACACTCCTATTGTCAAGGTCTAAATACATTAAAAACCTCATGTGTAATAGGCGTATAA  
TGATAACAGGTGACCAATGTTTTCTGAATGCATAAAGAAATGAATAAACTCAAACACAGTACTTCCATAACAA  
CTTCAACCAAAAAAGACCAAAACATGGAACGAATGGAAGCTTGTAAGGACATGCTTGTTTTAGTCCAGTGGTTT  
CCACAGCTGGCTAAGCCAGGAGTCACTTGAGGGCTTTTAAATACAAAACATTGGAGCTGGAGGCCATTATCCTT  
AGCAAATAATGCAGAAACAGAAAATCAACTACCGCATGTTCTCACTTATAAGTGGGAGGTAATGATAAGAAGT  
TATGAACACAAAGAAGGAAACAATAGACATTGGAGTCTATTTGAGAGGGGAGGGTGGGAGAAGGAAAAGGAGCA  
GAAAAGATAACTATTGAGTACTGCCTTCACACCTGGGTGATGAAATAATATGTACAACAAATCCCTGTGACACA  
TGTTTACCTATGGAACAAACCTTCATGTGTATCCCTAAACCTAAAATAAAAGTTAAAAAARAAAAA  
AAAAAARAAAAA  
AAAAAARAAAAA

318/330

**FIGURE 318**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA82361

&gt;&lt;subunit 1 of 1, 352 aa, 1 stop

&gt;&lt;MW: 38938, pI: 7.86, NX(S/T): 3

MALLLCFVLLCGVVDFAFARSLSITTPEEMIEKAKGETAYLPCKFTLSPEDQGPLDIEWLISPA  
DNQKVDQVIILYSGDKIYDDYYPDLKGRVHFTSNDLKSGDASINVTNLQLSDIGTYQCKVKK  
APGVANKKIHLLVVLVKPSGARCIVDGSEEIGSDFKIKCEPKESLPLQYEWQKLSDSQKMPT  
SWLAEMTSSVISVKNASSEYSGTYSCTVRNRVGSQCLLRNLNVVPPSNKAGLIAGAIIGTLL  
ALALIGLIIFCCRKKRREEKYEKEVHHDIREDVPPPKSRTSTARSYIGSNHSSLGSMSPSNM  
EGYSKTQYNQVPSSEDFERTPQSPTLPPAKFKYPYKTDGITVV

**Signal sequence.**

amino acids 1-19

**Transmembrane domain:**

amino acids 236-257

**N-glycosylation sites.**

amino acids 106-110, 201-205, 298-302

**Tyrosine kinase phosphorylation sites.**

amino acids 31-39, 78-85, 262-270

**N-myristoylation sites.**amino acids 116-122, 208-214, 219-225, 237-243, 241-247,  
245-251, 296-302**Myelin P0 protein.**

amino acids 96-125

319/330

**FIGURE 319**

TGAAATGACTTCCACGGCTGGGACGGGAACCTTCCACCCACAGCTATGCCTCTGATTGGTGA  
ATGGTGAAGGTGCCTGTCTAACTTTTCTGTAAAAAGAACCAGCTGCCTCCAGGCAGCCAGCC  
CTCAAGCATCACTTACAGGACCAGAGGGACAAGACATGACTGTGATGAGGAGCTGCTTTCGC  
CAATTTAACACCAAGAAGAATTGAGGCTGCTTGGGAGGAAGGCCAGGAGGAACACGAGACTG  
AGAG**ATG**AATTTTCAACAGAGGCTGCAAAGCCTGTGGACTTTAGCCAGACCCTTCTGCCCTC  
CTTTGCTGGCGACAGCCTCTCAAATGCAGATGGTTGTGCTCCCTTGCCTGGGTTTTACCCTG  
CTTCTCTGGAGCCAGGTATCAGGGGCCCAGGGCCAAGAATTCCACTTTGGGCCCTGCCAAGT  
GAAGGGGGTTGTTCCCCAGAACTGTGGGAAGCCTTCTGGGCTGTGAAAGACACTATGCAAG  
CTCAGGATAACATCACGAGTGCCCGGCTGCTGCAGCAGGAGGTTCTGCAGAACGTCTCGGAT  
GCTGAGAGCTGTTACCTTGTCCACACCCTGCTGGAGTTCTACTTGAAAAGTGTTCACAAAA  
CCACCACAATAGAACAGTTGAAGTCAGGACTCTGAAGTCATTCTCTACTCTGGCCAACAAC  
TTGTTCTCATCGTGTCAAACTGCAACCCAGTCAAGAAAATGAGATGTTTTCCATCAGAGAC  
AGTGCACACAGGCGGTTTTCTGCTATTCCGGAGAGCATTCAAACAGTTGGACGTAGAAGCAGC  
TCTGACCAAAGCCCTTGGGGAAGTGGACATTCTTCTGACCTGGATGCAGAAATTCTACAAGC  
TC**TGA**ATGTCTAGACCAGGACCTCCCTCCCCCTGGCACTGGTTTGTTCCTGTGTCAATTTCA  
AACAGTCTCCCTTCCTATGCTGTTCACTGGACACTTCACGCCCTTGGCCATGGGTCCCATTCT  
TTGGCCCAGGATTATTGTCAAAGAAGTCATTCTTTAAGCAGCGCCAGTGACAGTCAGGGGAAG  
GTGCCTCTGGATGCTGTGAAGAGTCTACAGAGAAGATTCTTGTATTTATTACAACTCTATTT  
AATTAATGTCAGTATTTCAACTGAAGTTCTATTTATTTGTGAGACTGTAAGTTACATGAAGG  
CAGCAGAATATTGTGCCCCATGCTTCTTTACCCCTCACAATCCTTGCCACAGTGTGGGGCAG  
TGGATGGGTGCTTAGTAAGTACTTAATAAACTGTGGTGCTTTTTTTGGCCTGTCTTTGGATT  
GTTAAAAAACAGAGAGGGATGCTTGGATGTAAACTGAACTTCAGAGCATGAAAATCACACT  
GTCTTCTGATATCTGCAGGGACAGAGCATTGGGGTGGGGGTAAGGTGCATCTGTTTGAAAAG  
TAAACGATAAAATGTGGATTAAAGTGCCCAGCACAAAGCAGATCCTCAATAAACATTTTCATT  
TCCCACCCACACTCGCCAGCTCACCCCATCATCCCTTTCCCTTGGTGCCCTCCTTTTTTTTTT  
TATCCTAGTCATTCTTCCCTAATCTTCCACTTGAGTGTCAAGCTGACCTTGCTGATGGTGAC  
ATTGCACCTGGATGTACTATCCAATCTGTGATGACATTCCCTGCTAATAAAAGACAACATAA  
CTCCAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

320/330

**FIGURE 320**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA88002

&gt;&lt;subunit 1 of 1, 206 aa, 1 stop

&gt;&lt;MW: 23799, pI: 9.12, NX(S/T): 3

MNFQQRLQSLWTLARPFCPPLLATASQMOMVVLPCLGFTLLLWSQVSGAQGQEFHFGPCQVK  
GVVPQKLWEAFWAVKDTMQAQDNITSARLLQQEVLQNVSDAESCYLEVHTLLEFYLKTVFKNH  
HNRTVEVRTLKSFSTLANNFVLIVSQLQPSQENEMFSIRDSAHRRFLLFRRAFKQLDVEAAL  
TKALGEVDILLTWMQKFYKL

**Signal sequence:**

amino acids 1-42

**N-glycosylation sites.**

amino acids 85-89, 99-103, 126-130

321/330

**FIGURE 321**

AAGGAGCAGCCCGCAAGCACCAAGTGAGAGGC**ATGA**AGTTACAGTGTGTTTCCCTTTGGCTC  
CTGGGTACAATACTGATATTGTGCTCAGTAGACAACCACGGTCTCAGGAGATGTCTGATTTC  
CACAGACATGCACCATATAGAAGAGAGTTTCCAAGAAATCAAAAGAGCCATCCAAGCTAAGG  
ACACCTTCCCAAATGTCACCTATCCTGTCCACATTGGAGACTCTGCAGATCATTAAAGCCCTTA  
GATGTGTGCTGCGTGACCAAGAACCTCCTGGCGTTCTACGTGGACAGGGTGTTCAGGATCA  
TCAGGAGCCAAACCCCAAAATCTTGAGAAAAATCAGCAGCATTGCCAACTCTTTCCTCTACA  
TGCAGAAAACCTCTGCGGCAATGTCAGGAACAGAGGCAGTGTCACTGCAGGCAGGAAGCCACC  
AATGCCACCAGAGTCATCCATGACAACTATGATCAGCTGGAGGTCCACGCTGCTGCCATTAA  
ATCCCTGGGAGAGCTCGACGTCTTTCTAGCCTGGATTAATAAGAATCATGAAGTAATGTTCT  
CAGCT**TGA**TGACAAGGAACCTGTATAGTGATCCAGGGATGAACACCCCCTGTGCGGTTTACT  
GTGGGAGACAGCCACCTTGAAGGGGAAGGAGATGGGGAAGGCCCTTGCAGCTGAAAGTCC  
CACTGGCTGGCCTCAGGCTGTCTTATTCCGCTTGAAAATAGGCAAAAAGTCTACTGTGGTAT  
TTGTAATAAACTCTATCTGCTGAAAGGGCCTGCAGGCCATCCTGGGAGTAAAGGGCTGCCTT  
CCCATCTAATTTATTGTAAAGTCATATAGTCCATGTCTGTGATGTGAGCCAAGTGATATCCT  
GTAGTACACATTGTACTGAGTGGTTTTTCTGAATAAATTCCATATTTTACCTATGA

322/330

**FIGURE 322**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA92282

&gt;&lt;subunit 1 of 1, 177 aa, 1 stop

&gt;&lt;MW: 20452, pI: 8.00, NX(S/T): 2

MKLQCVSLWLLGTILILCSVDNHGLRRCLISTDMHHIEESFQEIKRAIQAKDTFPNVTILST  
LETLQIIKPLDVCCVTKNLLAFYVDRVFKDHQEPNPKILRKISSIANSFLYMQKTLRQCQEQ  
RQCHCRQEATNATRVIHNDNYDQLEVHAAAIKSLGELDVFLAWINKNHEVMFSA

**Signal sequence:**

amino acids 1-18

**N-glycosylation sites.**

amino acids 56-60, 135-139

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 102-106

**N-myristoylation site.**

amino acids 24-30

**Actinin-type actin-binding domain signature 1.**

amino acids 159-169

323/330

**FIGURE 323**

CCCGTGCCAAGAGTGACGTAAGTACCGCCTATAGAGTCTATAGGCCCACTTGGCTTCGTTAG  
AACGCGGCTACAATTAATACATAACCTTATGTATCATAACATACGATTTAGGTGACACTAT  
AGAATAACATCCACTTTGCCTTTCTCTCCACAGGTGTCCACTCCCAGGTCCAACCTGCACCTC  
GGTTCTATCGATAATCTCAGCACCCAGCCACTCAGAGCAGGGCACG**ATG**TTGGGGGCCCCGCCT  
CAGGCTCTGGGTCTGTGCCTTGTGCAGCGTCTGCAGCATGAGCGTCCTCAGAGCCTATCCCA  
ATGCCTCCCCACTGCTCGGCTCCAGCTGGGGTGGCCTGATCCACCTGTACACAGCCACAGCC  
AGGAACAGCTACCACCTGCAGATCCACAAGAATGGCCATGTGGATGGCGCACCCCATCAGAC  
CATCTACAGTGCCCTGATGATCAGATCAGAGGATGCTGGCTTTGTGGTGATTACAGGTGTGA  
TGAGCAGAAGATACCTCTGCATGGATTTTCAGAGGCAACATTTTTGGATCACACTATTTTCGAC  
CCGGAGAACTGCAGGTTCCAACACCAGACGCTGGAAAACGGGTACGACGTCTACCACTCTCC  
TCAGTATCACTTCCTGGTCAGTCTGGGCCGGGCGAAGAGAGCCTTCTGCTGCCAGGCATGAACC  
CACCCCCGTACTCCCAGTTCCTGTCCCGGAGGAACGAGATCCCCCTAATTCACCTTCAACACC  
CCCATACCACGGCGGCACACCCGGAGCGCCGAGGACGACTCGGAGCGGGACCCCTGAACGT  
GCTGAAGCCCCGGGCCCCGGATGACCCCGGCCCCGGCCTCCTGTTACAGGAGCTCCCGAGCG  
CCGAGGACAACAGCCCGATGGCCAGTGACCCATTAGGGGTGGTCAGGGGCGGTTCGAGTGAAC  
ACGCACGCTGGGGGAACGGGCCCCGGAAGGCTGCCGCCCTTCGCCAAGTTCATC**TAG**GGTCTG  
CTGG



324/330

**FIGURE 324**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA142238

&gt;&lt;subunit 1 of 1, 251 aa, 1 stop

&gt;&lt;MW: 27954, pI: 9.22, NX(S/T): 1

MLGARLRLWVCALCSVCSMSVLRAYPNASPLLGSSWGGLIHLYTATARNSYHLQIHKNGHVD  
GAPHQTIYSALMIRSEDAGFVVITGVMSRRYLCMDFRGNIFGSHYFDPENCRFQHQTLENGY  
DVIHSPQYHFLVSLGRAKRAFLPGMNPPPYSQLSRNEIPLIHFNTPIPRRHTRSAEDDSE  
RDPLNVLKPRARMTPAPASCSQELPSAEDNSPMASDPLGVVRGGRVNTHAGGTGPEGCRPFA  
KFI

**Important features of the protein:****Signal peptide:**

amino acids 1-24

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 175-179

**N-myristoylation site.**

amino acids 33-39, 100-106, 225-231, 229-235

**HBGF/FGF family proteins**

amino acids 73-124

325/330

**FIGURE 325**

GGAAAAGGTACCCGCGAGAGACAGCCAGCAGTTCTGTGGAGCAGCGGTGGCCGGCTAGG**ATG**  
GGCTGTCTCTGGGGTCTGGCTCTGCCCCTTTTCTTCTTCTGCTGGGAGGTTGGGGTCTCTGG  
GAGCTCTGCAGGCCCCAGCACCCGCGAGAGCAGACACTGCGATGACAACGGACGACACAGAAG  
TGCCCGCTATGACTCTAGCACCGGGGCCACGCCGCTCTGGAAACTCAAACGCTGAGCGCTGAG  
ACCTCTTCTAGGGCCTCAACCCCAGCCGGCCCCATTCCAGAAGCAGAGACCAGGGGAGCCAA  
GAGAATTTCCCCTGCAAGAGAGACCAGGAGTTTCACAAAAACATCTCCCAACTTCATGGTGC  
TGATCGCCACCTCCGTGGAGACATCAGCCGCCAGTGGCAGCCCCGAGGGAGCTGGAATGACC  
ACAGTTCAGACCATCACAGGCAGTGATCCCGAGGAAGCCATCTTTGACACCCTTTGCACCGA  
TGACAGCTCTGAAGAGGCAAAGACACTCACAATGGACATATTGACATTGGCTCACACCTCCA  
CAGAAGCTAAGGGCCTGTCCTCAGAGAGCAGTGCCTCTTCCGACGGCCCCCATCCAGTCATC  
ACCCCGTCACGGGCCTCAGAGAGCAGCGCCTCTTCCGACGGCCCCCATCCAGTCATCACCCC  
GTCACGGGCCTCAGAGAGCAGCGCCTCTTCCGACGGCCCCCATCCAGTCATCACCCCGTCAT  
GGTCCCCGGGATCTGATGTCACCTCTCCTCGCTGAAGCCCTGGTGACTGTCACAAACATCGAG  
GTTATTAATTGCAGCATCACAGAAATAGAAACAACAACCTTCCAGCATCCCTGGGGCCTCAGA  
CATAGATCTCATCCCCACGGAAGGGGTGAAGGCCTCGTCCACCTCCGATCCACCAGCTCTGC  
CTGACTCCACTGAAGCAAAACCACACATCACTGAGGTCACAGCCTCTGCCGAGACCCTGTCC  
ACAGCCGGCACCACAGAGTCAGCTGCACCTCATGCCACGGTTGGGACCCCACTCCCCACTAA  
CAGCGCCACAGAAAGAGAAGTGACAGCACCCGGGGCCACGACCCTCAGTGGAGCTCTGGTCA  
CAGTTAGCAGGAATCCCCTGGAAGAAACCTCAGCCCTCTCTGTTGAGACACCAAGTTACGTC  
AAAGTCTCAGGAGCAGCTCCGGTCTCCATAGAGGCTGGGTCAGCAGTGGGCAAAACAACCTTC  
CTTTGCTGGGAGCTCTGCTTCCTCCTACAGCCCCCTCGGAAGCCGCCCTCAAGAACTTCACCC  
CTTCAGAGACACCGACCATGGACATCGCAACCAAGGGGCCCTTCCCCACCAGCAGGGACCCT  
CTTCCTTCTGTCCCTCCGACTACAACCAACAGCAGCCGAGGGACGAACAGCACCTTAGCCAA  
GATCACAACCTCAGCGAAGACCACGATGAAGCCCCAACAGCCACGCCCACGACTGCCCGGAC  
GAGGCCGACCACAGACG**TGA**GTGCAGGTGAAAATGGAGGTTTCCTCCTCCTGCGGCTGAGTG  
TGGCTTCCCCGGAAGACCTCACTGACCCCAGAGTGGCAGAAAGGCTGATGCAGCAGCTCCAC  
CGGGAACCTCCACGCCCACGCGCCTCACTTCCAGGTCTCCTTACTGCGTGTCAGGAGAGGCTA  
ACGGACATCAGCTGCAGCCAGGCATGTCCCGTATGCCAAAAGAGGGTGCTGCCCCTAGCCTG  
GGCCCCCACCAGACAGACTGCAGCTGCGTTACTGTGCTGAGAGGTACCCAGAAGGTTCCCATG  
AAGGGCAGCATGTCCAAGCCCCCTAACCCCAGATGTGGCAACAGGACCCTCGCTCACATCCAC  
CGGAGTGTATGTATGGGGAGGGGCTTACCTGTTCCCAGAGGTGTCTTGGACTCACCTTGG  
CACATGTTCTGTGTTTCAGTAAAGAGAGACCTGATCACCCATCTGTGTGCTTCCATCCTGCA  
TTAAAATTCACTCAGTGTGGCCCCAAAAAAA

326/330

**FIGURE 326**

MGCLWGLALPLFFFCWEVGVSGSSAGPSTRRADTAMTTDDTEVPAMTLAPGHAALETQTL  
ETSSRASTPAGPIPEAETRGAKRISPARETRSFTKTSPNFMVLIATSVETSAASGSPEGAGM  
TTVQITITGSDPEEAI FDTLCTDDSS EAKTLTMDILT LAHTSTEAKGLSSESSASSDGPHPV  
ITPSRASESSASSDGPHPVITPSRASESSASSDGPHPVITPSWSPGSDVTLLAEALVTVTNI  
EVINCSITEIETTTSSIPGASDIDLIPTEGVKASSTSDPPALPDSTEAKPHITEVTASAETL  
STAGTTESAAPHATVGTPLPTNSATEREVTAPGATTL SGALVTVSRNPLEETSALSVETPSY  
VKVSGAAPVSIEAGSAVGKTTSFAGSSASSYSPSEAALKNFTPSETPTMDIATKGPFPSTRD  
PLPSVPPTTTNSSRGTNSTLAKITTS AKTTMKPQQPRPRLPGRGRPQT

**N-glycosylation sites:**

amino acids 252-256, 445-449, 451-455

**cAMP-and cGMP-dependent protein kinase phosphorylation site.**

amino acids 84-90

**Casein kinase II phosphorylation sites.**

amino acids 37-41, 108-112, 131-135, 133-137, 148-152, 165-169,  
246-250, 254-258, 256-260, 269-273, 283-287, 333-337, 335-339,  
404-408, 414-418, 431-435

**N-myristoylation sites.**

amino acids 2-8, 19-25, 117-123, 121-127, 232-238, 278-284, 314-  
320, 349-355, 386-392, 397-403, 449-455

**ATP/GTP-binding site motif A (P-loop).**

amino acids 385-393

327/330

**FIGURE 327**

GCGGAGCATCCGCTGCGGTCTCGCCGAGACCCCCGCGCGGATTTCGCCGGTCCTTCCCGCGG  
GCGCGACAGAGCTGTCCTCGCACCTGGATGGCAGCAGGGGCGCCGGGGTCTCTCGACGCCA  
GAGAGAAATCTCATCATCTGTGCAGCCTTCTTAAAGCAAACCTAAGACCAGAGGGAGGATTAT  
CCTTGACCTTTGAAGACCAAACTAACTGAAATTTAAA**ATG**TTCTTCGGGGGAGAAGGGAG  
CTTGACTTACACTTTGGTAATAATTTGCTTCCTGACACTAAGGCTGTCTGCTAGTCAGAATT  
GCCTCAAAAAGAGTCTAGAAGATGTTGTTCATTGACATCCAGTCATCTCTTTCTAAGGGAATC  
AGAGGCAATGAGCCCGTATATACTTCAACTCAAGAAGACTGCATTAATTCTTGCTGTTCAAC  
AAAAAACATATCAGGGGACAAAGCATGTAACCTGATGATCTTCGACACTCGAAAAACAGCTA  
GACAACCCAACTGCTACCTATTTTTCTGTCCCAACGAGGAAGCCTGTCCATTGAAACCAGCA  
AAAGGACTTATGAGTTACAGGATAATTACAGATTTTCCATCTTTGACCAGAAATTTGCCAAG  
CCAAGAGTTACCCAGGAAGATTCTCTCTTACATGGCCAATTTTCACAAGCAGTCACTCCCC  
TAGCCCATCATCACACAGATTATTCAAAGCCCACCGATATCTCATGGAGAGACACACTTTCT  
CAGAAGTTTGGATCCTCAGATCACCTGGAGAACTATTTAAGATGGATGAAGCAAGTGCCCA  
GCTCCTTGCTTATAAGGAAAAAGGCCATTCTCAGAGTTTACAATTTTCTCTGATCAAGAAA  
TAGCTCATCTGCTGCCTGAAAATGTGAGTGCCTCCAGCTACGGTGGCAGTTGCTTCTCCA  
CATAACACCTCGGCTACTCCAAAGCCCGCCACCCTTCTACCCACCAATGCTTCAGTGACACC  
TTCTGGGACTTCCCAGCCACAGCTGGCCACCACAGCTCCACCTGTAACCACTGTCACCTTCTC  
AGCCTCCCACGACCCTCATTTCTACAGTTTTTACACGGGCTGCGGCTACACTCCAAGCAATG  
GCTACAACAGCAGTTCTGACTACCACCTTTCAGGCACCTACGGACTCGAAAGGCAGCTTAGA  
AACCATAACGTTTACAGAAATCTCCAACCTTAACCTTGAACACAGGGAATGTGTATAACCTA  
CTGCACTTTCTATGTCAAATGTGGAGTCTTCCACTATGAATAAACTGCTTCTGCGGAAGGT  
AGGGAGGCCAGTCCAGGCAGTTCTTCCCAGGGCAGTGTTCCAGAAAATCAGTACGGCCTTCC  
ATTTGAAAAATGGCTTCTTATCGGGTCCCTGCTCTTTGGTGTCTGTTCTGCTGGTGATAGGCC  
TCGTCCTCCTGGGTAGAATCCTTTCGGAATCACTCCGCAGGAAACGTTACTCAAGACTGGAT  
TATTTGATCAATGGGATCTATGTGGACATC**TAA**GGATGGAACCTCGGTGTCTCTTAATTCATT  
TAGTAACCAGAAGCCCAAATGCAATGAGTTTCTGCTGACTTGCTAGTCTTAGCAGGAGGTTG  
TATTTTGAAGACAGGAAAATGCCCCCTTCTGCTTTCCTTTTTTTTTTTGGAGACAGAGTCTT  
GCTCTGTTGCCAGGCTGGAGTGCAGTAGCACGATCTCGGCTCTCACCGCAACCTCCGTCTC  
CTGGGTTCAAGCGATTCTCCTGCCTCAGCCTCCTAAGTATCTGGGATTACAGGCATGTGCCA  
CCACACCTGGGTGATTTTTGTATTTTGTAGTAGAGACGGGGTTTACCATGTTGGTCAGGCTG  
GTCTCAAACCTCCTGACCTAGTGATCCACCCTCCTCGGCCTCCCAAAGTGCTGGGATTACAGG  
CATGAGCCACCACAGCTGGCCCCCTTCTGTTTTATGTTTGGTTTTTTGAGAAGGAATGAAGTG  
GGAACCAAATTAGGTAATTTTGGGTAATCTGTCTCTAAAATATTAGCTAAAAACAAAGCTCT  
ATGTAAAGTAATAAAGTATAATTGCCATATAAATTTCAAATTCAACTGGCTTTTATGCAAA  
GAAACAGGTTAGGACATCTAGGTTCCAATTCATTCACATTCTTGGTTCCAGATAAAATCAAC  
TGTTTATATCAATTTCTAATGGATTTGCTTTTCTTTTATATGGATTCCTTTAAACCTTATT  
CCAGATGTAGTTCCTTCCAATTAAATATTTGAATAAATCTTTTGTTACTCAA

328/330

**FIGURE 328**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA45410

&gt;&lt;subunit 1 of 1, 431 aa, 1 stop

&gt;&lt;MW: 46810, pI: 6.45, NX(S/T): 6

MFFGGEGSLTYTLVIICFLTLRLSASQNCLKKSLEDVVIDIQSSLKGIKRGNEPVYTSTQED  
CINSCCSTKNISGDKACNLMIFDTRKTARQPNCYLFFCPNEEACPLKPAKGLMSYRIITDFP  
SLTRNLPSQELPQEDSLLHGQFSQAVTPLAHHHTDYSKPTDISWRDTLSQKFGSSDHLEKLF  
KMDEASAQLLAYKEKGHSQSSQFSSDQEIAHLLPENVSALPATVAVASPHTTSATPKPATLL  
PTNASVTPSGTSQPQLATTAPPVTTVTSPPTTLISTVFTRAAATLQAMATTAVLTTTTFQAP  
TDSKGSLETIPFTEISNLTNTGNVYNPTALSMSNVESSTMNKTASWEGREASPGSSSQGSV  
PENQYGLPFEKWLLIGSLLFGVLFLVIGLVLLGRILSESLRRKRYRLDYLINGIYVDI

**Signal sequence.**

amino acids 1-25

**Transmembrane domain.**

amino acids 384-405

**N-glycosylation sites.**

amino acids 72-76, 222-226, 251-255, 327-331, 352-356

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 415-419

**Tyrosine kinase phosphorylation site.**

amino acids 50-57

**N-myristoylation sites.**

amino acids 4-10, 48-54, 315-321

329/330

**FIGURE 329**

CTCCACGGTGTCCAGCGCCCAGAA**ATG**CGGCTTCTGGTCCTGCTATGGGGTTGCCTGCTGCT  
CCCAGGTTATGAAGCCCTGGAGGGGCCAGAGGAAATCAGCGGGTTCGAAGGGGACACTGTGT  
CCCTGCAGTGCACCTACAGGGAAGAGCTGAGGGACCACCGGAAGTACTGGTGCAGGAAGGGT  
GGGATCCTCTTCTCTCGCTGCTCTGGCACCATCTATGCAGAAGAAGAAGGCCAGGAGACAAT  
GAAGGGCAGGGTGTCCATCCGTGACAGCCGCCAGGAGCTCTCGCTCATTGTGACCCTGTGGA  
ACCTCACCCCTGCAAGACGCTGGGGAGTACTGGTGTGGGGTCGAAAAACGGGGCCCCGATGAG  
TCTTTACTGATCTCTCTGTTTCGTCTTTCCAGGACCCTGCTGTCTCTCCCTCCCCTTCTCCCAC  
CTTCCAGCCTCTGGCTACAACACGCCTGCAGCCCCAAGGCAAAGCTCAGCAAACCCAGCCCC  
CAGGATTGACTTCTCCTGGGCTCTACCCGGCAGCCACCACAGCCAAGCAGGGGAAGACAGGG  
GCTGAGGCCCCCTCCATTGCCAGGGACTTCCCAGTACGGGCACGAAAGGACTTCTCAGTACAC  
AGGAACCTCTCCTCACCCAGCGACCTCTCCTCCTGCAGGGAGCTCCCGCCCCCCCCATGCAGC  
TGGACTCCACCTCAGCAGAGGACACCAGTCCAGCTCTCAGCAGTGGCAGCTCTAAGCCCAGG  
GTGTCCATCCCGATGGTCCGCATACTGGCCCCAGTCTGGTGCTGCTGAGCCTTCTGTGAGC  
CGCAGGCCTGATCGCCTTCTGCAGCCACCTGCTCCTGTGGAGAAAGGAAGCTCAACAGGCCA  
CGGAGACACAGAGGAACGAGAAGTTCTGGCTCTCACGCTTGACTGCGGAGGAAAAGGAAGCC  
CCTTCCCAGGCCCTGAGGGGGACGTGATCTCGATGCCTCCCCTCCACACATCTGAGGAGGA  
GCTGGGCTTCTCGAAGTTTGTCTCAGCG**TAG**GGCAGGAGGCCCTCCTGGCCAGGCCAGCAGT  
GAAGCAGTATGGCTGGCTGGATCAGCACCGATTCCCGAAAGCTTTCCACCTCAGCCTCAGAG  
TCCAGCTGCCCGGACTCCAGGGCTCTCCCCACCCTCCCCAGGCTCTCCTCTTGATGTTCCA  
GCCTGACCTAGAAGCGTTTGTGAGCCCTGGAGCCCAGAGCGGTGGCCTTGCTCTTCCGGCTG  
GAGACTGGGACATCCCTGATAGGTTTACATCCCTGGGCAGAGTACCAGGCTGCTGACCCTCA  
GCAGGGCCAGACAAGGCTCAGTGGATCTGGTCTGAGTTTCAATCTGCCAGGAACCTCTGGGC  
CTCATGCCCAGTGTGCGACCCTGCCTTCTCCCACTCCAGACCCACCTTGTCTTCCCTCCC  
TGGCGTCTCAGACTTAGTCCCACGGTCTCCTGCATCAGCTGGTGATGAAGAGGAGCATGCT  
GGGGTGAGACTGGGATTCTGGCTTCTCTTTGAACCACCTGCATCCAGCCCTTCAGGAAGCCT  
GTGAAAAACGTGATTCTTGGCCCCACCAAGACCCACCAAAAACCATCTCTGGGCTTGGTGCAG  
GACTCTGAATTCTAACAATGCCCAGTGAAGTGTGCACTTGAGTTTGAGGGCCAGTGGGCCTG  
ATGAACGCTCACACCCCTTCAGCTTAGAGTCTGCATTTGGGCTGTGACGTCTCCACCTGCCC  
CAATAGATCTGCTCTGTCTGCGACACCAGATCCACGTGGGGACTCCCCTGAGGCCTGCTAAG  
TCCAGGCCTTGGTCAGGTCAGGTGCACATTGCAGGATAAGCCCAGGACCGGCACAGAAGTGG  
TTGCCTTTNCCATTTGCCCTCCCTGGNCCATGCCTTCTTGCCCTTTGGAAAAAATGATGAAGA  
AAACCTTGGCTCCTTCTTGTCTGGAAAGGGTTACTTGCCTATGGGTTCTGGTGGCTAGAGA  
GAAAAGTAGAAAACCAGAGTGCACGTAGGTGTCTAACACAGAGGAGAGTAGGAACAGGGCGG  
ATACCTGAAGGTGACTCCGAGTCCAGCCCCCTGGAGAAGGGGTGCGGGGTGGTGGTAAAGTA  
GCACAACTACTATTTTTTTTCTTTTTCCATTATTATTGTTTTTTAAGACAGAATCTCGTGCT  
GCTGCCCAGGCTGGAGTGCAGTGGCACGATCTGCAAACCTCCGCCTCCTGGGTTCAAGTGATT  
CTTCTGCCTCAGCCTCCCGAGTAGCTGGGATTACAGGCACGCACCACCACACCTGGCTAATT  
TTTGTACTTTTAGTAGAGATGGGGTTTCACCATGTTGGCCAGGCTGGTCTTGAACCTCTGAC  
CTCAAATGAGCCTCCTGCTTCAGTCTCCCAAATTGCCGGGATTACAGGCATGAGCCACTGTG  
TCTGGCCCTATTTCTTTAAAAAGTGAAATTAAGAGTTGTTTCAGTATGCAAACTTGGAAG  
ATGGAGGAGAAAAAGAAAAGGAAGAAAAAATGTCACCCATAGTCTCACCAGAGACTATCAT  
TATTTTCGTTTTGTGTACTTCTTCCACTCTTTTCTTCTTACATAATTTGCCGGTGTTCTT  
TTTACAGAGCAATTATCTTGTATATACAACTTTGTATCCTGCCTTTTCCACCTTATCGTTCC  
ATCACTTTATTCCAGCACTTCTCTGTGTTTTACAGACCTTTTTATAAATAAAATGTTTCATCA  
GCTGCATAAAAAAAAAAAAAA

330/330

**FIGURE 330**

&lt;/usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA44196

&lt;subunit 1 of 1, 332 aa, 1 stop

&lt;MW: 36143, pI: 5.89, NX(S/T): 1

MRLLVLLWGCLLLPGYEALEGP EEISGFEGDTVSLQCTYREELRDHRKYWCRKGGILFSRCS  
GTIYAEEEGQETMKGRVSIRDSRQELSLIVTLWNLTLDAGEYWCGVEKRGPD ELLISLFV  
FPGPCCPPSPSPTFQPLATTRLQPKAKAQQQTQPPGLTSPGLYPAATTAKQGKTGA EAPPLPG  
TSQYGHERTSQYTGTSPHPATSP PAGSSRPPMQLDSTSAEDTSPALSSGSSKPRVSIPMVRI  
LAPVLVLLSLLSAAGLIAFCSHLLLRKEAQQATETQRNEKFWLSRLTAE EKEAPSQAPEGD  
VISM PPLHTSEEELGFSKFVSA

**Important features:****Signal peptide:**

amino acids 1-17

**Transmembrane domain:**

amino acids 248-269

**N-glycosylation site.**

amino acids 96-99

**Fibrinogen beta and gamma chains C-terminal domain.**

amino acids 104-113

**Ig like V-type domain:**

amino acids 13-128

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/08439

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/47 C07K14/705 C12N15/62 C07K16/18  
 G01N33/53 A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

STRAND

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 39448 A (HUMAN GENOME SCIENCES INC) 11 September 1998 (1998-09-11) see passages relating to gene 174 (clone H2MBF44) and the claims. ---	1-28
X	WO 98 42741 A (GENETICS INST) 1 October 1998 (1998-10-01) see passages relating to clone ck181_7 and the claims. ---	1-28
A	EP 0 834 563 A (SMITHKLINE BEECHAM CORP) 8 April 1998 (1998-04-08) the whole document ---	
A	WO 97 07198 A (GENETICS INST) 27 February 1997 (1997-02-27) the whole document ---	
	--- -/--	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## ° Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance  
 "E" earlier document but published on or after the international filing date  
 "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  
 "O" document referring to an oral disclosure, use, exhibition or other means  
 "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

16 August 2000

Date of mailing of the international search report

13.11.00

Name and mailing address of the ISA

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Authorized officer

Smalt, R



## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	YOKOYAMA-KOBAYASHI M ET AL: "A signal sequence detection system using secreted protease activity as an indicator" GENE,NL,ELSEVIER BIOMEDICAL PRESS. AMSTERDAM, vol. 163, no. 2, 3 October 1995 (1995-10-03), pages 193-196, XP004041983 ISSN: 0378-1119 the whole document	
A	--- KLEIN R D ET AL: "Selection for genes encoding secreted proteins and receptors" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA,US,NATIONAL ACADEMY OF SCIENCE. WASHINGTON, no. 93, 1 July 1996 (1996-07-01), pages 7108-7113, XP002077277 ISSN: 0027-8424 the whole document	
P,X, L	--- WO 99 63088 A (BAKER KEVIN ;CHEN JIAN (US); GENENTECH INC (US); YUAN JEAN (US); G) 9 December 1999 (1999-12-09) see passages relating to PR0281 and the claims. L: priority.	1-28
P,X	--- WO 99 46375 A (SCHMITT ARMIN ;SPECHT THOMAS (DE); DAHL EDGAR (DE); HINZMANN BERND) 16 September 1999 (1999-09-16) see whole document, particularly passages relating to seq.ID'2 219 and 251	1-13, 17-28
P,X	--- WO 99 53040 A (SCHMITT ARMIN ;SPECHT THOMAS (DE); DAHL EDGAR (DE); HINZMANN BERND) 21 October 1999 (1999-10-21) page 1 -page 8 see claims. page 128	1-13, 17-22, 24-28
P,X	--- WO 00 08145 A (NOVARTIS ERFINDUNGEN VERWALTUN ;NOVARTIS AG (CH); HOLNESS CLAIRE L) 17 February 2000 (2000-02-17) the whole document	1-13, 21-28
P,X	--- WO 99 63083 A (TSURITANI KATSUKI ;ARASE SEIJI (JP); IKEDA AKIKO (JP); TAISHO PHAR) 9 December 1999 (1999-12-09) abstract see sequences.	1-13,21, 22,25-28
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# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/08439

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Claims 1-28, All partially.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: Invention 1: claims 1-28, all partially

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0281 (seq.ID.2), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR0281, chimeric protein comprising a portion corresponding to PR0281, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto.

2. Claims: Inventions 2-132: claims 1-28,  
all partially and claims 4 and 13 as far as  
applicable

Subject matter as defined for invention 1 above, but limited to the respective amino acid sequences and corresponding nucleic acid sequences referred to as:

2. PR0276 (seq.ID's 5/6),
3. PR0189 (Seq.ID's 7/8),
4. PR0190 (Seq.ID's 13/14),
5. PR0341 (Seq.ID's 19/20),
6. PR0180 (Seq.ID's 22/23),
7. PR0190 (Seq.ID's 13/14),
8. PR0194 (Seq.ID's 27/28),
9. PR0203 (Seq.ID's 29/30),
10. PR0290 (Seq.ID's 32/33),
11. PR0874 (Seq.ID's 35/36),
12. PR0710 (Seq.ID's 40/41),
13. PR01151 (Seq.ID's 46/47),
14. PR01281 (Seq.ID's 51/52),
15. PR0358 (Seq.ID's 56/57),
16. PR01310 (Seq.ID's 61/62),
17. PR0698 (Seq.ID's 66/67),
18. PR0732 (Seq.ID's 72/73),
19. PR01120 (Seq.ID's 83/84),
20. PR0537 (Seq.ID's 94/95),
21. PR0536 (Seq.ID's 96/97),
22. PR0535 (Seq.ID's 98/99),
23. PR0718 (Seq.ID's 102/103),
24. PR0872 (Seq.ID's 112/113),
25. PR01063 (Seq.ID's 114/115),
26. PR0619 (Seq.ID's 116/117),
27. PR01188 (Seq.ID's 123/124),
28. PR0784 (Seq.ID's 134/135),
29. PR0783 (Seq.ID's 137/138),
30. PR0820 (Seq.ID's 145/146),

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

31. PR01080 (Seq.ID's 147/148),
32. PR01079 (Seq.ID's 150/151),
33. PR0793 (Seq.ID's 152/153),
34. PR01016 (Seq.ID's 155/156),
35. PR01013 (Seq.ID's 157/158),
36. PR0937 (Seq.ID's 159/160),
37. PR0842 (Seq.ID's 164/165),
38. PR0839 (Seq.ID's 166/167),
39. PR01180 (Seq.ID's 168/169),
40. PR01134 (Seq.ID's 170/171),
41. PR0830 (Seq.ID's 174/175),
42. PR01115 (Seq.ID's 176/177),
43. PR01277 (Seq.ID's 178/179),
44. PR01135 (Seq.ID's 180/181),
45. PR0828 (Seq.ID's 188/189),
46. PR01009 (Seq.ID's 193/194),
47. PR01007 (Seq.ID's 196/197),
48. PR01056 (Seq.ID's 198/199),
49. PR0826 (Seq.ID's 200/201),
50. PR0819 (Seq.ID's 202/203),
51. PR01006 (Seq.ID's 204/205),
52. PR01112 (Seq.ID's 206/207),
53. PR01074 (Seq.ID's 208/209),
54. PR01005 (Seq.ID's 210/211),
55. PR01073 (Seq.ID's 212/213),
56. PR01152 (Seq.ID's 215/216),
57. PR01136 (Seq.ID's 218/219),
58. PR0813 (Seq.ID's 220/221),
59. PR0809 (Seq.ID's 222/223),
60. PR0791 (Seq.ID's 224/225),
61. PR01004 (Seq.ID's 226/227),
62. PR01111 (Seq.ID's 228/229),
63. PR01344 (Seq.ID's 230/231),
64. PR01109 (Seq.ID's 235/236),
65. PR01383 (Seq.ID's 240/241),
66. PR01003 (Seq.ID's 245/246),
67. PR01108 (Seq.ID's 247/248),
68. PR01137 (Seq.ID's 249/250),
69. PR01138 (Seq.ID's 252/253),
70. PR01054 (Seq.ID's 255/256),
71. PR0994 (Seq.ID's 257/258),

## 3. Claim : 1

72. PR0812 (Seq.ID's 259/260),
73. PR01069 (Seq.ID's 261/262),
74. PR01129 (Seq.ID's 263/264),
75. PR01068 (Seq.ID's 265/266),
76. PR01066 (Seq.ID's 267/268),
77. PR01184 (Seq.ID's 269/270),
78. PR01360 (Seq.ID's 271/272),
79. PR01029 (Seq.ID's 273/274),
80. PR01139 (Seq.ID's 275/276),
81. PR01309 (Seq.ID's 277/278),

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

82. PR01028 (Seq.ID's 280/281),
83. PR01027 (Seq.ID's 282/283),
84. PR01107 (Seq.ID's 284/285),
85. PR01140 (Seq.ID's 286/287),
86. PR01106 (Seq.ID's 288/289),
87. PR01291 (Seq.ID's 290/291),
88. PR01105 (Seq.ID's 292/293),
89. PR0511 (Seq.ID's 294/295),
90. PR01104 (Seq.ID's 296/297),
91. PR01100 (Seq.ID's 298/299),
92. PR0836 (Seq.ID's 300/301),
93. PR01141 (Seq.ID's 302/303),
94. PR01132 (Seq.ID's 308/309),
95. PR01346 (Seq.ID's 313/314),
96. PR01131 (Seq.ID's 318/319),
97. PR01281 (Seq.ID's 325/326),
98. PR01064 (Seq.ID's 333/334),
99. PR01379 (Seq.ID's 339/340),
100. PR0844 (Seq.ID's 344/345),
101. PR0848 (Seq.ID's 346/347),
102. PR01097 (Seq.ID's 348/349),
103. PR01153 (Seq.ID's 350/351),
104. PR01154 (Seq.ID's 352/353),
105. PR01182 (Seq.ID's 356/357),
106. PR01155 (Seq.ID's 358/359),
107. PR01156 (Seq.ID's 360/361),
108. PR01098 (Seq.ID's 362/363),
109. PR01127 (Seq.ID's 364/365),
110. PR01126 (Seq.ID's 366/367),
111. PR01125 (Seq.ID's 368/369),
112. PR01186 (Seq.ID's 370/371),
113. PR01198 (Seq.ID's 372/373),
114. PR01158 (Seq.ID's 374/375),
115. PR01159 (Seq.ID's 376/377),
116. PR01124 (Seq.ID's 378/379),
117. PR01287 (Seq.ID's 380/381),
118. PR01312 (Seq.ID's 386/387),
119. PR01192 (Seq.ID's 388/389),
120. PR01160 (Seq.ID's 393/394),
121. PR01187 (Seq.ID's 398/399),
122. PR01185 (Seq.ID's 400/401),
123. PR01345 (Seq.ID's 402/403),
124. PR01245 (Seq.ID's 407/408),
125. PR01358 (Seq.ID's 409/410),
126. PR01195 (Seq.ID's 411/412),
127. PR01270 (Seq.ID's 413/414),
128. PR01271 (Seq.ID's 415/416),
129. PR01375 (Seq.ID's 417/418),
130. PR01385 (Seq.ID's 419/420),
131. PR01384 (Seq.ID's 423/424),
132. PR09828 (Seq.ID's 510/511).

For the sake of conciseness, the first subject matter is explicitly defined, the other subject matters are defined by analogy thereto.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

4. Claims: Invention 133: claims 1-36,69-74,99-102,  
all partially and claims 4 and 13 as far as  
applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0943 (seq.ID.118), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR0943, chimeric protein comprising a portion corresponding to PR0943, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR0183, PR0184 or PR0185 through interaction with PR0943 and vice versa, method of linking a bioactive molecule to a cell expressing PR0943 using PR0183, PR0184 or PR0185 as binding ligands and vice versa, and method of modulating the activity of PR0943 by binding with PR0183, PR0184 or PR0185, and vice versa.

5. Claims: Inventions 134-136: claims 1-36,69-74,99-102,  
all partially and claims 4 and 13 as far as  
applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0183 (seq.ID.495), PR0184 (seq.ID.497) or PR0185 (seq.ID.499), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR0183, PR0184 or PR0185 through interaction with PR0943 and vice versa, method of linking a bioactive molecule to a cell expressing PR0943 using PR0183, PR0184 or PR0185 as binding ligands and vice versa, and method of modulating the activity of PR0943 by binding with PR0183, PR0184 or PR0185, and vice versa, whereby invention 134 is limited to PR0183, invention 135 is limited to PR0184, and invention 136 is limited to PR0185.

6. Claims: Invention 137: claims 1-28,37-44,75-80,103-106,  
all partially and claims 4 and 13 as far as  
applicable

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0331 (seq.ID.501), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR0331, chimeric protein comprising a portion corresponding to PR0331, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR01133 through interaction with PR0331 and vice versa, method of linking a bioactive molecule to a cell expressing PR0331 using PR01133 as binding ligands and vice versa, and method of modulating the activity of PR0331 by binding with PR01133, and vice versa.

7. Claims: Invention 138: claims 1-28,37-44,75-80,103-106,  
all partially and claims 4 and 13 as far as  
applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR01133 (seq.ID.129), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR01133 through interaction with PR0331 and vice versa, method of linking a bioactive molecule to a cell expressing PR0331 using PR01133 as binding ligands and vice versa, and method of modulating the activity of PR0331 by binding with PR01133, and vice versa.

8. Claims: Invention 139: claims 1-28,45-52,81-86,107-110,  
all partially and claims 4 and 13 as far as  
applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR01387 (seq.ID.422), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR01387, chimeric protein comprising a portion corresponding to PR01387, antibody against said protein, the isolated extracellular domain of said protein or a protein with at

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR0363 or PR05723 through interaction with PR01387 and vice versa, method of linking a bioactive molecule to a cell expressing PR01387 using PR0363 or PR05723 as binding ligands and vice versa, and method of modulating the activity of PR01387 by binding with PR0363 or PR05723, and vice versa.

9. Claims: Invention 140 and 141: claims 1-28,45-52,81-86, 107-110,  
all partially and claims 4 and 13 as far as applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0363 (seq.ID.503) or PR05723 (seq.ID.505), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR0363 or PR05723 through interaction with PR01387 and vice versa, method of linking a bioactive molecule to a cell expressing PR01387 using PR0363 or PR05723 as binding ligands and vice versa, and method of modulating the activity of PR01387 by binding with PR0363 or PR05723, and vice versa, whereby invention 140 is limited to PR0363 and invention 141 is limited to PR05723.

10. Claims: Invention 142: claims 1-28, 53-60,87-92,111-114,  
all partially and claims 4 and 13 as far as applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR01114 (seq.ID.183), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR01114, chimeric protein comprising a portion corresponding to PR01114, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR03301 or PR09940 through interaction with PR01114 and vice versa, method of linking a bioactive molecule to a cell expressing PR01114 using PR03301 or PR09940 as binding ligands and vice versa,



## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

and method of modulating the activity of PR01114 by binding with PR03301 or PR09940, and vice versa.

11. Claims: Invention 143 and 144: claims 1-28, 53-60,87-92, 111-114,  
all partially and claims 4 and 13 as far as applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR03301 (seq.ID.507) or PR09940 (seq.ID.509), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR03301 or PR09940 through interaction with PR01114 and vice versa, method of linking a bioactive molecule to a cell expressing PR01114 using PR03301 or PR09940 as binding ligands and vice versa, and method of modulating the activity of PR01114 by binding with PR03301 or PR09940, and vice versa, whereby invention 143 is limited to PR03301 and invention 144 is limited to PR09940.

12. Claims: Invention 145: claims 1-28,61-69,93-98,115-118,  
all partially and claims 4 and 13 as far as applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR01181 (seq.ID.355), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR01181, chimeric protein comprising a portion corresponding to PR01181, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR07170, PR0361 or PR0846 through interaction with PR01181 and vice versa, method of linking a bioactive molecule to a cell expressing PR01181 using PR07170, PR0361 or PR0846 as binding ligands and vice versa, and method of modulating the activity of PR01181 by binding with PR07170, PR0361 or PR0846, and vice versa.

13. Claims: Inventions 146-148: claims 1-28,61-69,93-98,

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

115-118,  
all partially and claims 4 and 13 as far as  
applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR07170 (seq.ID.513), PR0361 (seq.ID.515) or PR0846 (seq.ID.517), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR07170, PR0361 or PR0846 through interaction with PR01181 and vice versa, method of linking a bioactive molecule to a cell expressing PR01181 using PR07170, PR0361 or PR0846 as binding ligands and vice versa, and method of modulating the activity of PR01181 by binding with PR07170, PR0361 or PR0846, and vice versa, whereby invention 146 is limited to PR07170, invention 147 is limited to PR0361, and invention 148 is limited to PR0846.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/08439

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9839448 A	11-09-1998	AU 6545398 A EP 0972029 A EP 0972030 A WO 9839446 A	22-09-1998 19-01-2000 19-01-2000 11-09-1998
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WO 9963083 A	09-12-1999	JP 11332571 A AU 3955099 A	07-12-1999 20-12-1999